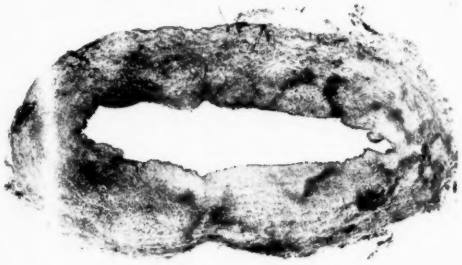

Fig. 4. Transverse section, dog 1.

Fig. 5. Transverse section, dog 24.

TECHNIQUE

Group I. A rubber tube French catheter No. 8 or No. 10 was introduced into the common bile duct through a small incision. The tube was passed upward and was fixed there by tying a ligature about the duct and the tube, or by placing a suture on either side of the duct so as to include in it the tube and the duct. The lower end of the tube was made to pass along the duct through the papilla of Vater into the lumen of duodenum. A variable amount of the duct wall was now destroyed. Since it was not possible to measure accurately the width of the defect because the tube forced the edges of the wound apart, an attempt was made to estimate the width of the defect in terms of percentages of the circumference of the duct. The length could be readily measured. The defect was covered by a flap of the gastrohepatic omentum pulled under the posterior aspect of the bile duct and laid over the defect. A few interrupted sutures were employed to fix the flap in place so as to make a complete omental tube about the defect (Fig. 1, a and b). This step was found to be quite useful later in recognizing the reconstructed duct in postmortem examination. The adherent omental flap indicated the area (Figs. 1 and 2). The length of the defect in the group was usually from just below the cystic duct down to the superior border of duodenum, almost the entire length of the supraduodenal portion of the duct. The width of the defect was from 50 to 70 per cent of the circumference of the duct, in several instances only a narrow posterior strip of the duct wall being left.

Group II. Essentially the same technique was employed, the defect varying from that of a mere longitudinal slit in the anterior wall to not more than 40 per cent of the circumference of the duct.

Group III. This group was carried out according to Sullivan's technique. A rubber tube was introduced into the common bile duct and was fixed there just below the cystic duct by a suture made to pass through the tube and the duct on each side of the duct. The duct was resected below the sutures and the lower stump at the border of duodenum was ligated with silk. The tube running freely exposed in the peritoneal cavity was laid upon the superior anterior wall of the first part of the duodenum to which it was now fixed for about a distance of 1½ to 2 centimeters after the manner of Witzel's gastrostomy technique. The lower end of the tube was introduced into the lumen of the bowel through a stab. Omental tissue drawn from the lesser omentum, the greater omentum, or both, was used to make a tubular investment for the exposed tube (Fig. 1, a and b).

Group IV. Cuff excision. A rubber tube was introduced as in the previous group. This tube was secured just below the cystic duct by a suture on either side of it. Another pair of sutures fixed it to the duct just above the superior border of duodenum. The intervening duct was cut away. The gap was covered by an omental flap.

ANALYSIS OF RESULTS

Results were analyzed in the light of the following points:

1. Occurrence of ascending infection.

Fig. 6. High power photomicrograph, dog 25.

2. Incidence of stenosis and its relation to the ascending infection.

3. Influence of tube remaining *in situ* on the occurrence of ascending infection.

4. Epithelial regeneration in four groups.

5. Relation of inflammation in wall of reconstructed duct to epithelial regeneration.

6. Relation of stenosis to epithelial regeneration.

7. Adhesions of duodenum to the liver and its effect upon the length of the new duct.

Total number of dogs operated on was 130.

Fig. 7. Adhesion of duodenum to under surface of liver.

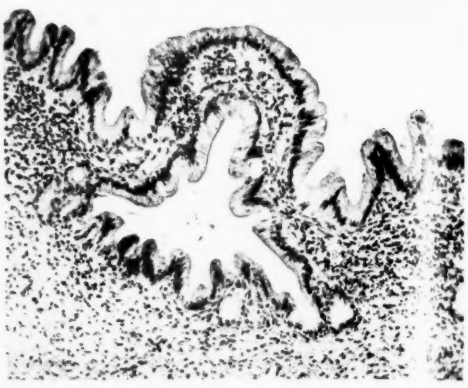

Fig. 8. Photomicrographic section showing normal tissue.

The number of successful experiments was 28. Group I—10 dogs; Group II—6 dogs; Group III—10 dogs, and Group IV—2 dogs.

Of a total of 28 dogs, 5 did not develop an ascending infection. Eight exhibited a high grade of infection and in 15 it was mild. The severe grades of ascending infection were characterized either by acute lesions, such as purulent cholecystitis, purulent cholangeitis with multiple liver abscesses, or by more chronic lesions, such as a thickened gall bladder or a hobnailed liver.

The milder grades of ascending infection manifested themselves by the presence of adhesions between the gall bladder and the diaphragm, the stomach, duodenum, etc. The gall bladder was frequently enlarged, its walls thickened, and the characteristic slate blue color changed to a whitish or greyish. It was interesting to note in these cases the presence of milky radiating scars on the surface of the liver, so called subcapsular scars considered characteristic of a gall bladder infection in man. They were most prominent over that area of liver overlying the gall bladder. These subcapsular scars were seen only at a post-mortem examination never at operation.

When we examine the relation of ascending infection to stenosis, we find that all of the animals exhibiting stenosis likewise exhibited an ascending infection. In Group I dogs 3, 8, and 24 did not develop a stenosis of the reconstructed duct. Dogs 3 and 24 did not exhibit any evidence of an ascending infection and

dog 8 a very mild one. In Group II dogs 6, 14, and 20 did not develop duct stenosis and in dogs 14 and 20 no ascending infection was evident. When we examine Group III, we find that while dogs 16, 21, and 22 had no stenosis, only dog 16 did not exhibit signs of an ascending infection. Dog 22 had a mild and dog 21 a severe infection in the absence of a stenosis. From this it is apparent that while stenosis never failed to be associated with an ascending infection, its absence did not save dogs 8, 19, and 22 from a mild, and dogs 6 and 21 from a severe infection. Furthermore, in dogs 19, 21, and 22 the tube did not pass. The contention of Museneeck that the presence of the tube in the duct is a safeguard against an ascending infection because it prevents stenosis, is, therefore, incorrect. While the tube prevented stenosis it was not able to prevent an ascending infection in dogs 19, 21, and 22. It may be assumed that the responsible factor in the 5 dogs without stenosis was interference with the closing mechanism of the sphincter of Oddi.

The question of epithelial regeneration: That ductal epithelium possesses a capacity for regeneration could be safely assumed *a priori* on purely biological considerations. It is well known that epithelial liver cells as well as epithelial cells lining intrahepatic ductus biliferi possess a high degree of regenerative power. However, it is likewise known that under certain conditions these cells perish and fail to regenerate. Our query, therefore, should be not so much, can the ductal epithelium regenerate, but rather, can it regenerate under certain conditions?

In Group I there were extensive defects running almost the entire length of the supraduodenal portion of the choledochus and involving from 50 to 70 per cent of the circumference of the duct. Of 10 dogs, 4 showed complete epithelial regeneration; 6, none.

In Group II, with small defects running from a longitudinal slit to defects not larger than 40 per cent of the circumference, all of the ducts healed by epithelial proliferation.

The Sullivan group, consisting of 10 dogs, did not exhibit, in a single instance, any epithelial ingrowth in the new channel—this, despite the fact that the new channel in each was much shorter than the reconstructed duct at the time of operation (Fig. 3).

In Group IV one dog showed no epithelial regeneration and the other showed a markedly hypertrophic epithelial lining. However, I believe it to be old epithelium. The duodenum was adherent to the liver shortening up the original duct to one-half its original length. The amount of duct resected was 2 centimeters. It is easy to see that the stumps of the resected duct became approximated in that way. Furthermore, young, recently regenerated epithelium does not exhibit such marked papillary evagination as did this one.

If we enquire further into the question of why in Group I 4 ducts displayed complete epithelial regeneration while in 6 there was none, we find a ready answer in the histological picture of these ducts.

Dog 3, with a large defect in the common bile duct, had an uneventful recovery. The animal never exhibited jaundice, its nutrition was good and general health perfectly normal. It was sacrificed exactly one year after the operation. At postmortem examination the peritoneum was found to be normal. The first portion of the duodenum was adherent to the liver. Liver, stomach, and duodenum were removed together. The duodenum was slit open on its mesenteric side. The tube was not to be seen. The papilla was visualized and a sound introduced into it passed upward into the hilus of the liver without meeting any obstruction. The common bile duct appeared smooth, somewhat larger than normal, and whitish in appearance. All of the supraduodenal portion of the duct was removed for histological study. Transverse serial sections were made and were stained with hæmatoxylin and eosin. In all of the sections the epithelial regeneration was practically complete. The original epithelium was readily recognized by its marked papillary evagination and a marked tendency to formation of parietal sacculi. The new epithelium was rather poorly developed. There was no evidence of inflammatory reaction in the wall of the regenerated duct. Gall bladder sections and liver sections appeared normal.

Dog 8. The duct was very fine. After introduction into it of an ureteral catheter No. 6, all that was left of the duct was a strip of the posterior wall. The defect was covered by an omental flap. The work was considered unsatisfactory. The dog, however, remained in good condition and was sacrificed 106 days later. On postmortem examination, the peritoneum was found to be normal. The gall bladder was pinkish-grey. Its fundus was attached to the dome of the diaphragm by a broad adhesion. The first portion of the duodenum was adherent to the inferior aspect of the right lobe of the liver. On the surface

of the liver were seen milky, radiating, subcapsular scars. Liver, stomach, and duodenum were removed *en masse* and laid on the table for more detailed study. The duodenum was opened on its mesenteric side. Pressure on the gall bladder caused thick bile to flow from the papilla. A probe passed up without encountering any obstruction. The duct appeared somewhat larger than normal, felt thicker, and presented a smooth glistening appearance. Transverse sections of the duct showed complete epithelial regeneration. The epithelium was quite normal. It displayed papillary evaginations and parietal sacculi (Fig. 2). Comparison with a normal duct of a dog (Fig. 4) demonstrates that there is no inflammatory reaction in the wall of the regenerated duct.

As a contrast to dogs 3 and 8, I shall present the history of dog 1.

Dog 1. The same operation was performed here as in dogs 3 and 8. Three weeks after the operation the animal exhibited signs of biliary obstruction, but these had disappeared, and the animal remained in a fair state of nutrition. He was sacrificed 106 days after the operation. Postmortem examination showed the following: The liver was much enlarged. There were firm adhesions between the liver, duodenum, and stomach. All visible extrahepatic ducts were tremendously enlarged. Liver, stomach, and duodenum were removed together and the duodenum and stomach were slit open. Pressure on the fundus of the gall bladder caused a watery, viscous fluid to exude from the papilla. A probe passed up the papilla became arrested just above the superior border of the duodenum. The duct above the constriction was tremendously enlarged. The point of obstruction corresponded to the site of the lower ligature tied about the duct and the tube. The supraduodenal portion of the duct was removed for histological study. Transverse sections showed the lumen of the duct for the greater part, at least 70 per cent of it, devoid of any epithelial lining. Whatever epithelium there was exhibited poor development, total absence of papillary evaginations and of gland formation. The duct wall itself was tremendously hypertrophied. It consisted of enormous amounts of connective tissue. Here and there were to be seen areas of marked infiltration with polymorphonuclear leucocytes (Fig. 4).

Dog 2. In this animal there was not a trace of epithelium. The wall was of extraordinary thickness.

The same histological picture was found in all 6 animals which did not show any epithelial regeneration. The ducts which healed by epithelial proliferation exhibited in all four instances a wall of approximately the thickness of a normal duct. Conclusion may be drawn from Groups I and II that ductal epithelium is capable of growing and filling in small as well as extensive longitudinal defects, provided that its blood supply is not compromised by an excessive inflammatory process. Excessive reaction with its superabundant connective tissue undergoes a later contracture with the development of a stenosis. There was no instance of epithelial regeneration in the presence of a stenosis in all of the series save one. This exception was dog 13 in Group IV. However, as pointed out before, we were dealing here most likely with old epithelium brought together rather than with new epithelium.

Epithelial growth is influenced more by an adequate blood supply than by the extent of the defect. This was strikingly demonstrated in dogs 24 and 25 of Group I. In dog 24 the defect amounted to 1.7 centimeters in length by 70 per cent of the circumference. It was sacrificed 95 days later. There was no evidence of an ascending infection, or of stenosis. Epithelial regeneration was complete. The duct wall showed no inflammatory reaction (Fig. 5, dog 24).

Dog 25. The defect was smaller than in dog 24. It amounted to 1.5 centimeters in length by 50 per cent of the circumference. It was sacrificed 81 days after operation. Mild stenosis of the duct was present. There were gross signs of a mild ascending infection, such as a thickened gall bladder, subcapsular scars on the liver surface, and a hobnailed appearance of the liver. A partly healed gastric ulcer was found. Histological sections demonstrated that epithelium was absent in many parts, and that, wherever present, it was poorly developed. The duct wall was abnormally thick and consisted of bundles of connective tissue. These were seen to surround epithelial glands. One could easily see how later contracture would choke the epithelial elements (Fig. 6).

In the Sullivan group of 10 dogs, there was not a single instance of epithelial proliferation in the new channel. The same was true of Group IV. Therefore, it is evident that epithelium will not grow along a prosthesis to fill a transverse gap. How can we explain the successful results of Jenckel, Verhoogen, and Wilms? Verhoogen's case was repeated in dogs 4 and 13. I feel that I am justified in rejecting the theory of epithelial proliferation along the prosthesis on the basis of postmortem evidence of Desplas and on the basis of my results with the Sullivan group. Explanation must be sought in the formation of

adhesions between the duodenum, pylorus, and the liver. The effect of this phenomenon is obvious. It shortens materially the gap to be bridged. It is easy to see that in Verhoogen's case the stumps of the duct were brought together in just this manner. It would be difficult, if not impossible, to explain the *modus operandi* of repair except on this basis. Cahen was first to call attention to the rôle played by these adhesions in the description of the postmortem examination of his patient, in 1913. Museneeck emphasized its occurrence in experimental work. In my own material it took place in all but 1 animal (dog 24). The length of the duct in this dog appeared unusual. I have made an attempt to measure the length of the choledochus at the time of operation and again at postmortem, but this was impossible because of adhesions and altered relations. It would, however, be no exaggeration to state that the new ducts were markedly shortened. In the dog the duodenum is freely movable. Furthermore, in my work it was necessary to hold and exert some pull upon the first portion of the duodenum in order to expose the free edge of the hepatoduodenal ligament. Mechanical trauma, with perhaps some spilling of bile, furnished sufficient irritation to produce adhesions. While in reality a mild pathological complication, it no doubt played a most favorable part in the outcome of successful cases (Fig. 7).

Duodenal and gastric ulceration in dogs with stenosis of the common bile duct: That the exclusion of bile from the intestine may lead to development of duodenal or gastric ulcers has been recently pointed out by Kapsinow, Kim and Ivy, Berg and Jobling, and others. I was not familiar with this fact until an acute perforation of a duodenal ulcer in dog 5 forcibly called my attention to it. Observations on this point were made in 20 animals. Nine developed stenosis and of these 9, 7 had ulcers. Duodenal ulcer occurred alone four times, gastric alone twice, duodenal and gastric once. There was one perforation. The incidence of occurrence was 78 per cent. All of the animals exhibited more or less hepatitis.

The cause of ulceration may be at least in part due to interference with the process of alkalinization of acid chyme by the bile. There is evidence to believe that hepatitis may play an important part in the causation of these ulcers.

CONCLUSIONS

1. Epithelium lining the extrahepatic bile ducts is capable of regeneration under favorable conditions.

2. Small longitudinal defects will heal readily by epithelial regeneration; a fact familiar to the clinical surgeon and borne out by the experiments in Group II.

3. Longitudinal defects, even if extensive, may regenerate under favorable conditions, namely, in the absence of marked inflammatory reaction in its walls, as demonstrated by Group I.

4. Ductal epithelium is not capable of growing along a prosthesis and lining a gap, as was demonstrated by Groups III and IV.

5. Obstruction to the flow of bile invariably leads to an ascending infection. The presence of a tube in the bile duct, even with the absence of a stenosis, leads to infection presumably by interfering with the mechanism of the sphincter of Oddi.

6. Diversion in dogs of bile from the duodenum results in a high percentage of duodenal and gastric ulcerations invariably accompanied by a hepatitis.

7. Dogs die in from 24 to 48 hours from the effect of spilling bile into the peritoneal cavity without signs of peritonitis.

8. Omental covering is the ideal safeguard against bile leakage and infection.

9. Excessive inflammatory reaction at the site of repair is prejudicial to epithelial growth. (The use of absorbable suture material and omission of drain would tend to minimize such reaction.)

10. The Jenckel-Sullivan or Wilms-Brewer operation can be regarded only as a measure of necessity justified under certain desperate conditions rather than as operation of choice. Formation of adhesions with their subsequent contracture and pulling up of the duodenum to the porta hepatis is the more plausible explanation of the *modus operandi* of healing in an occasional successful case, than the problematic growth of ductal epithelium along a prosthesis or new channel.

SUMMARY

Causes leading to stenosis of the extrahepatic bile ducts were discussed and clinical evidence regarding their regenerative capacity educed. From the analysis of the results of various methods of reconstruction, it is apparent that the stumbling block to success is the question of adequate blood supply to the new channel. That is particularly true of the method of fistula implantation and also of flap methods. The method of bridging a gap with a rubber tube was given particular consideration. Clinical evidence regarding its efficacy was found to be contradictory. Adherents of the method concluded that success was explainable on the basis of extraordinary regenerative capacity of ductal epithelium. The epithelium, they believed, grew along the prosthesis and lined the new channel.

The question of regenerative capacity of ductal epithelium was studied experimentally. It was found that epithelium will proliferate and fill longitudinal defects, even if extensive, provided there be no excessive inflammatory reaction at the site of repair. The question of blood supply to the epithelium was again found to be the determining factor. It was found that epithelium will not grow along a tube and will not regenerate a transverse gap. This experience coincides with the postmortem evidence of clinical cases.

Importance of adhesions as a factor in favorable outcome was emphasized. This idea receives its support from the observations of Cahen, Lahey, Museneeck, and my own experimental work. There is no one satisfactory method, at the present time, of dealing successfully with cases of extensive bile duct obliteration in which direct anastomosis is not possible.

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CARCINOMA OF THE ŒSOPHAGUS[1]

WILLIAM L. WATSON, M.D., F.A.C.S., NEW YORK
Assistant Attending Surgeon, Memorial Hospital

THE problems presented by tumors of the œsophagus have engaged the attention of many capable surgeons, pathologists, internists, and endoscopists during the past 30 years. The radiologist, being concerned with the diagnostic and the treatment phases of the problem, has had a twofold interest in the disease. This widespread interest has led to the accumulation of considerable literature on the subject.

Much original thought, experimentation, and imagination have gone into the development of the many varied forms of treatment which have been advocated at one time or another for the cure of cancer of the œsophagus. Noteworthy among these methods was the advent of radium as an intra-œsophageal method of irradiation. This method was first proposed in 1904 and soon the literature was quite flooded with descriptions of new apparatus, new dosages, new filters, and new methods for accurately locating the radium in the œsophagus. This period, begun so hopefully, was not, however, followed by reports of cures or even good palliative results and the method fell somewhat into disfavor.

A great deal of attention had been directed toward the development of a procedure for radical removal of carcinoma located in the œsophagus. In several of the larger European clinics some significant results had been obtained in the removal of the cervical and intra-abdominal portions of the œsophagus for carcinoma. The first successful intrathoracic œsophagectomy was accomplished in this country by Torek in 1913. With this success œsophageal surgery was thought to have reached a point where it could be called the answer to the treatment problem. Unfortunately, surgery has not fulfilled its early promise. Such a general lack of success would lead one to suspect that those who have advocated these various methods of treatment have been unjustifiably optimistic.

A careful study of the clinical course of the disease, the anatomy of the organ involved, and the postmortem material available will show that patients with cancer of the œsophagus should be given palliative treatment as a routine measure and that only in the very unusual early case should intra-œsophageal irradiation or radical surgery be attempted. The cured case will be a medical curiosity.

The material for this report has been taken from the Memorial Hospital records accumulated during the 13 year period between 1918 and 1931. Five hundred and six (506) patients with carcinoma of the œsophagus were admitted to the hospital and of this number there were 267 patients with positive biopsy diagnoses. For the past several years all patients have had biopsies removed for diagnosis. Previously this was considered an unnecessary risk, and, for this reason, biopsies were seldom taken from the early patients. The entire material of 506 cases has been summarized in this report, but the statistical portion is based on a study of only those cases with positive microscopical sections. To include the cases without biopsy would be quite justifiable, but would not appreciably alter the statistics and might lead to some criticism as to the accuracy of the figures.

Twenty-nine patients suffering from œsophageal obstruction thought to be cancer were admitted and later their obstruction was proved to be due to such benign causes as spasm, syphilis, non-specific ulcer, acid or alkali burns, and idiopathic stenosis. Most of these patients recovered under appropriate dilatation measures.

An intimate knowledge of the anatomy of the œsophagus is necessary in order to understand the dangers and difficulties encountered in the treatment of cancer in this organ. The œsophagus is a thin walled tube about 25 centimeters in length, developed from the foregut. It differs from the other portions of the intestinal tract in that it lacks an outer serosal covering, a distinct surgical disadvantage. The œsophagus is richly supplied with lymphatics in the submucosal and muscular coats,

[1] From the Department of Head and Neck Surgery, Memorial Hospital.

thus providing a submucous pathway for the dissemination of cancer. Mucus forming glands are found throughout the œsophagus and undoubtedly give rise to the adenocarcinomata which occur in this organ. The œsophagus is surrounded throughout its length by important and vital structures (Fig. 1) which are invaded early in the course of œsophageal cancer.

GROSS PATHOLOGICAL ANATOMY

Gross examination of a number of œsophageal carcinoma specimens demonstrates three definite types: First, there is the bulky, polypoid, projecting, or vegetative type which usually grows into the lumen of the œsophagus causing obstructive symptoms at a relatively early stage (Fig. 2). Second, there is the shallow, ulcerating type causing early symptoms of mediastinal involvement such as pain and backache (Fig. 3). Metastases and obstructive symptoms may be absent. This type tends to perforate the musculature of the œsophagus early and to invade the aorta, bronchi, or trachea. Perforation into one of these vital structures causes death, most often by sudden hæmorrhage due to the perforation of the aorta or other large vessels (Carr, Polson and McIntosh, Heitzmann). Third, there is the hard, infiltrating, scirrhous type which invades the œsophageal wall, and which may encircle the lumen causing fixation of the walls and producing symptoms of obstruction. It may be superficially ulcerated (Fig. 4). The extension of the disease by way of the submucous lymphatics is shown in Figure 5. Here we find an outcropping of tumor tissue several centimeters above the primary growth.

Œsophageal growths are usually divided into another three groups according to their location in the upper, middle, or lower third of the œsophagus. Recently it has become the custom to locate the lesion by its relation to the various anatomical constrictions of the œsophagus. This method is more accurate than the former. Table I shows the relative frequency of cancer of the œsophagus at the three levels.

The most plausible reason for the relatively high frequency at the lower third (about 50 per cent) is the increased irritation due to the slowing of hot liquids at the diaphragmatic constriction and to the frequent presence of chronic spasm in this location.

TABLE I.—DISTRIBUTION OF GROWTHS

Authority	Cases reported	Upper ⅓		Middle ⅓		Lower ⅓	
		Cases	Per cent	Cases	Per cent	Cases	Per cent
Kraus	857	158	18.4	302	35.2	397	46.3
Janeway and Green	1630	256	15	527	32	847	52
Memorial Hospital series	245	46	18.8	67	27.3	132	53.8

MICROPATHOLOGY

In the Memorial Hospital series of 267 cases there were 243 squamous cell lesions, 19 adenocarcinomata, and 5 of the transitional cell type. The adenocarcinomata were all located in the lower third of the œsophagus. Guisez reported a series of 1,413 cases, five-sixths of which were squamous cell carcinomata and one-sixth adenocarcinomata. He did not once encounter a sarcoma. Jackson reported 671 cases of which 316 were adenocarcinomata, all located in the lower third of the œsophagus; 2 lymphosarcomata; 2 round cell carcinomata; and the remainder, 337 cases, squamous cell carcinomata.

With 267 positive biopsies it was found that the material was suitable for grading in 227 cases. This work was done largely by Dr. F. W. Stewart. Table II shows the relative frequency of the different grades and the number of cases which were diagnosed as histologically susceptible to radiation. In this series it is seen that there were only 39 cases (12.7 per cent) in the grade 3 group, 14 (6.1 per cent) of which were reported as probably radiation sensitive. Only 30 of the cases (13.2 per cent) in the grade 2 group were probably radiation sensitive. About 18 per cent of the carcinomata of the œsophagus are radiation sensitive. This evidence does not agree with Guisez's impression that œsophageal cancers are as a rule susceptible to radiation. There were no cases in the grade 4 group. Figure 6 shows photomicrographs of the three grades of carcinoma which occur in the œsophagus.

Broders and Vinson reported 220 cases with 90 per cent in groups 3 and 4 and no grade 1

TABLE II.—RELATIVE FREQUENCY OF GRADES

	Cases	Radiation sensitive
Grade 1	15	0
Grade 2	148	30
Grade 3	39	14
Adenocarcinoma	19	..
Transitional cell	6	..
Totals	227	44

cases. In the Memorial Hospital series 83 per cent of the cases fell in the groups 2 and 3.

AUTOPSY FINDINGS

Most of our cases are hospitalized for a short time only. For this reason the autopsy material is limited to 27 cases. Thirteen cases (48 per cent) coming to postmortem showed no evidence of metastasis. It must be borne in mind, however, that a careful autopsy does not always demonstrate the presence of early metastatic deposits. There was gross lymph-node involvement in 12 (44 per cent) of the 27 cases (Fig. 7). In 7 cases (26 per cent) there was extension to, or actual rupture into, the trachea or bronchus. In 2 cases (7 per cent) the disease ruptured into the aorta causing sudden fatal hæmorrhage. Pneumonia was a contributory cause of death in 13 cases (48 per cent); 12 were bronchopneumonias, and 1 was lobar in type. In 4 cases hæmorrhage was the cause of death. Other causes were peritonitis, 3 cases; starvation, asphyxia, cardiovascular disease, generalized carcinomatosis, septicæmia, and diarrhœa, each 1 case. In one case the cause of death was not determined due to a limited autopsy permit.

ETIOLOGY

It is not possible to give exact etiological data. However, it is now quite generally believed that there are certain definite factors which predispose to œsophageal new-growths. In the oral cavity it has been shown that broken, irregular, or sharply worn teeth, ill fitting plates, leucoplakia, excessive pipe smoking, syphilis, and intra-oral sepsis are definitely irritating factors in the causation of intra-oral carcinoma. Similar factors prepare the œsophageal mucous membrane for cancerous changes. Badly kept teeth, intra-oral sepsis, and ill-fitting plates tend to cause hasty and incomplete mastication which makes it necessary for the œsophagus to handle masses of food which are large and hard. A large, hard bolus of food causes a certain amount of trauma and inflammation of the œsophageal mucous membrane. The passage downward of such a bolus of food would be slowest at the point of anatomical constriction and the resulting trauma would be greatest at these points. This trauma causes irritation which may lead to spasm, and with it further slowing of the food bolus and later stagnation, œsophagitis, ulceration, and possibly tumor.

Thermal irritation is probably the most constant factor predisposing to carcinomata of the œsophagus. The frequent drinking of copious amounts of excessively hot tea is a history frequently obtained from the Russian patient suffering from cancer of the œsophagus. This fact is especially significant when it is seen that 46 per cent of the foreign patients in our series were born in Russia. There were more Russians than native born patients (Fig. 8). In China, cancer of the œsophagus is very uncommon among the women. This is said to be due to the fact that they eat after the men have finished and the rice is not so hot. The women of Scotland drink excessively hot tea and Turner has reported that cancer of the œsophagus is more common with them than it is among the men.

Leucoplakia of the œsophagus is being recognized more frequently due to the increasing popularity of the œsophagoscope. It is a very common condition. Schaer found it to be present in 60 per cent of 200 non-cancerous cases coming to autopsy. Clinically and pathologically the process is the same as that seen in the oral cavity (Sharp) where it is a definite etiological factor.

Guisez, who has had a very extensive experience with œsophageal cancer, thinks the excessive use of alcohol, spiced food, and tobacco are factors in many of his cases. He has noted also that the onset of cancer of the œsophagus is often definitely attributed by the patient to some particular mental or physical shock. He observed an increase in the incidence of cancer of the œsophagus in young adults following the World War and thought the following sequence of events had taken place: first an emotional upset; then an œso-

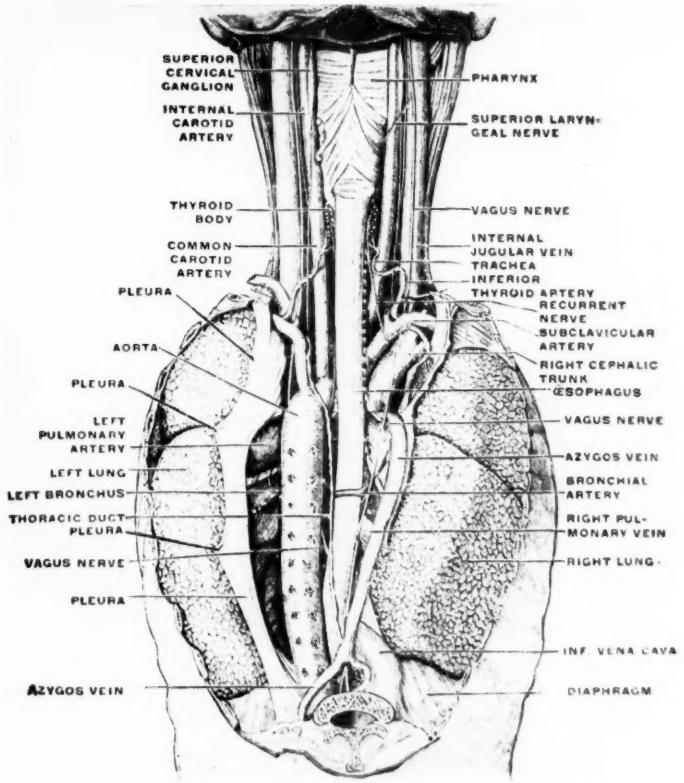

Fig. 1. Showing the position and relation of the œsophagus in the cervical region and in the posterior mediastinum. Seen from behind. (From Poirier and Charpy.)

phageal spasm, followed by stasis, œsophagitis, contracture, or inflammatory stenosis; and finally cancer. Jackson has pointed out the fact that cancer of the œsophagus often occurs in patients who have had œsophageal spasm for years. Guisez reported 70 such cases.

Mosher has demonstrated the presence of thin webs and pouches in the œsophagus. These may have an etiological bearing as may also the cicatricial contractures which result from the swallowing of caustic solutions or the healing of peptic or traumatic ulcers.

Syphilis does not play an important rôle in the etiology of the disease. It was present in only 7 per cent of our cases. Lamy found syphilis present in 10 per cent of his cases and Jackson reported 14 positive Wassermann reactions in his 671 cases (2 per cent). Cases of carcinoma of the œsophagus have been reported in which luetic or tubercular lesions co-existed. One case reported by Dean and Gregg showed cancer, syphilis, and tuberculosis of the œsophagus. Syphilis is present in the general run of the population in about the same proportion as it was in our series of cancer cases.

INCIDENCE

Cancer of the œsophagus makes up slightly more than 2.5 per cent of all the cases admitted to Memorial Hospital with malignant disease (Pack and LeFevre). In New York City during the year 1931 there were 8,336 deaths caused by cancer. Of these 282 were due to cancer of the œsophagus, an incidence

Fig. 2.

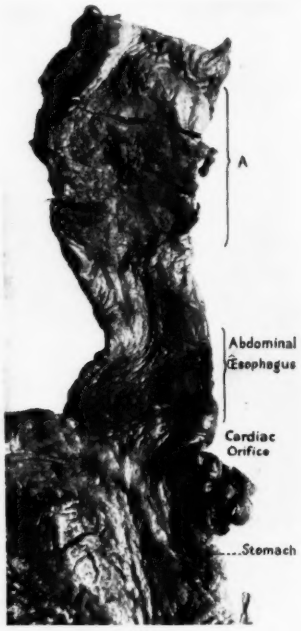

Fig. 3.

Fig. 4.

Fig. 2. Postmortem specimen showing large bulky squamous carcinoma of the œsophagus invading the trachea. Bronchopneumonia was the cause of death in this case.

Fig. 3. A large shallow ulcerating carcinoma of the œsophagus at its lower third. Microscopic section of the lesion showed squamous carcinoma, grade 2, radiation resistant.

Fig. 4. An œsophageal cancer of the middle third. Microscopic section showed squamous carcinoma, grade 3.

of 3.38 per cent. Abel reports that cancer of the œsophagus makes up 5 per cent of all cancer cases, Ernst 6 to 10 per cent, and Litten 8.29 per cent. It is amazing that this very fatal disease should have such a high incidence. The figures, I believe, will appear high even to one actively engaged in cancer work.

SEX

It is well known that this disease is much more common in the male sex. Guisez, with 1,430 cases, reported 6 males to 1 female. Jackson, with 671 cases, reported 87 per cent males, and in our series of 267 cases there were 225 males (84.3 per cent) and 52 females (15.7 per cent) (Figs. 9 and 10).

AGE

The youngest patient with proved carcinoma of the œsophagus treated at the Memorial Hospital was 35 years old and the oldest was a man of 80. The average age of the females was 53.8 years while the average for the males was 57.4 years. Cummins first called attention to the fact that the female sex developed carcinoma of the œsophagus at an earlier period of life than did the male. Our figures agree fully with his findings.

SYMPTOMATOLOGY

The onset of carcinoma of the œsophagus is most insidious, and, although we have the ready means (œsophagoscopy) for making a positive diagnosis, it is still a fact that one seldom sees a patient in the early stages of this disease. The function of the œsophagus is to transport food from the pharynx to the stomach and this function is seriously interfered with only late in the course of the disease. Then, too, the patient will masticate

his food more thoroughly after he notices that large particles of food have a tendency to stop or "stick" part way down. Such periods of temporary dysphagia tell a story to the physician, but, unfortunately, the patient pays little heed to such a matter and will mention it only when a careful history is obtained.

When definite persistent dysphagia occurs and the patient seeks relief for it, his disease is usually quite advanced. It is most unfortunate that dysphagia should so often be the first symptom of œsophageal new-growth. In our series 64 per cent of the patients gave as their first symptom difficulty in swallowing solid foods. If the mortality from this disease is to be reduced, earlier diagnoses must be made and earlier symptoms must be sought for and detected. When dysphagia, dehydration, and emaciation exist, the disease is hopelessly advanced. Dysphagia is not an invariable finding in œsophageal carcinoma; it may be absent in patients dying of the disease (Cabot-Emanuel). In cases of so called "cardiospasm" and other nervous disorders, dysphagia may be present for 20 years or more unrelated to malignant disease in the œsophagus. Dysphagia is thus an unreliable symptom and of little aid in making an early diagnosis.

The following vague, early, but less frequent symptoms noted in this series seem worth mentioning in the interests of early diagnosis. A feeling of substernal pressure was complained of in 6 cases; anorexia, 4 cases; feeling of obstruction, 4 cases; hiccoughs, 2 cases; hoarseness, 2 cases; difficulty in breathing, heartburn, and increased mucus in the throat, each 1 case. Foul breath is a common symptom.

The œsophagus is not supplied with sensory nerve fibers and is in itself insensible to pain so that when backache, substernal discomfort, or pain do exist it follows that the disease has extended beyond the œsophageal walls into the posterior mediastinum. Hoarseness when present is usually due to paralysis of the left side of the larynx caused by involvement of the left recurrent nerve. Regurgitation, vomiting, loss of weight, weakness, and pain are all symptoms of a late stage of the disease. Janeway, Jackson, Torek, Guisez, and many others interested in this work have made pleas for earlier diagnosis, but the early symptomatology is too vague to be of much help in this direction.

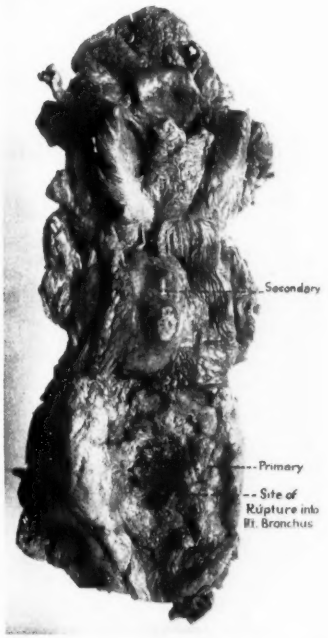

Fig. 5. Gross specimen showing a large primary carcinoma of the œsophagus perforating into the right bronchus causing death by asphyxia. A large secondary growth 5 centimeters in diameter is seen several centimeters above the primary lesion. Microscopic section showed the lesion to be an epidermoid carcinoma, grade 3.

DIAGNOSIS

That the diagnosis of this disease may be completely missed has been shown by Cabot who reported 3,000 autopsies among which were 20 cases of carcinoma of the œsophagus. In 4 of these cases the diagnosis had not been made, and in 3 it was merely suspected. This was a higher percentage of mistakes than occurred in any other disease. Œsophagoscopy is more popular now than it was in 1912 when Cabot made his report, and undoubtedly the percentage of missed diagnoses has been reduced by that procedure.

Kussmaul in 1868 was the first to realize œsophagoscopy by passing a rigid, straight,

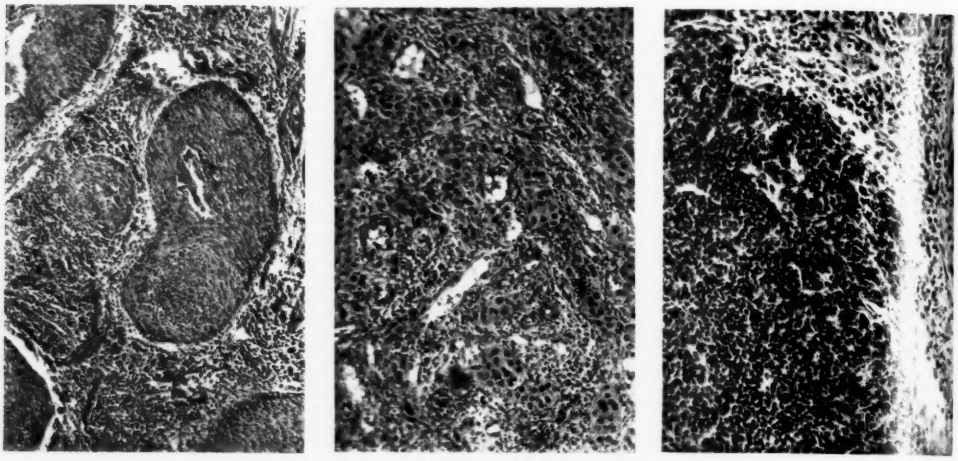

Fig. 6. Photomicrographs showing the three grades of squamous carcinoma found in the œsophagus.

steel tube into the person of a professional sword swallower at Freiburg. Mikulicz in 1881 showed that œsophagoscopy was a feasible procedure, but for the next 35 years there was steady opposition to the practice. Many cases of perforation and death were reported, and this state of affairs continued up to comparatively recent years when the technique was made quite safe and the procedure became popular.

It must be emphasized that œsophagoscopy is absolutely necessary for the making of an early and accurate diagnosis. Complicated apparatus, difficult roentgen-ray technique, and various opaque mixtures have been developed with the idea of making an early roentgen-ray diagnosis possible, but these have lost their popularity due to the more satisfactory œsophagoscopic results.

The following diagnostic procedures are carried out at the Memorial Hospital: The patient's history is obtained and he is given a general physical examination. He is then referred to the Head and Neck Department where the oral cavity and larynx are carefully examined and blood drawn for a Wassermann test. Following this he is sent for fluoroscopy and barium swallowing, and then X-ray films of the œsophagus and lungs are taken. With the data obtained on hand, the pharynx is cocainized, an œsophagoscopy is done, and a biopsy obtained. Biopsies are now taken in all uncomplicated cases.

Fluoroscopy is essential for a complete examination because by this means we are able to observe the function of the œsophagus. The procedure also determines the following points as regards cancer in this organ: size, shape, outline, and position of the lesion; size and shape of the lumen above and below the obstruction; the presence or absence of small marginal defects (Ernst); and fistulæ and lung complications. This data is of utmost value in determining what form of treatment should be instituted. The œsophagoscopist if possible should be present during the roentgen-ray examination of his patient. By the use of a heavy, thick, opaque mixture and the taking of X-ray films of the patient in several different positions, it is possible to obtain a film such as that shown in Figure 11, which gives an accurate picture of the lesion—its position, shape, and size.

Of 203 cases in which the patients were examined roentgenologically, positive X-ray diagnoses of carcinoma were returned in 97 cases, obstruction in 47 cases, constriction or stricture in 21 cases, filling defect in cases, irregularity in 8 cases, evidence of ulceration in 1 case. In no case was the lesion missed. Jackson reported a positive biopsy in each case diagnosed as cancer by his roentgenologist.

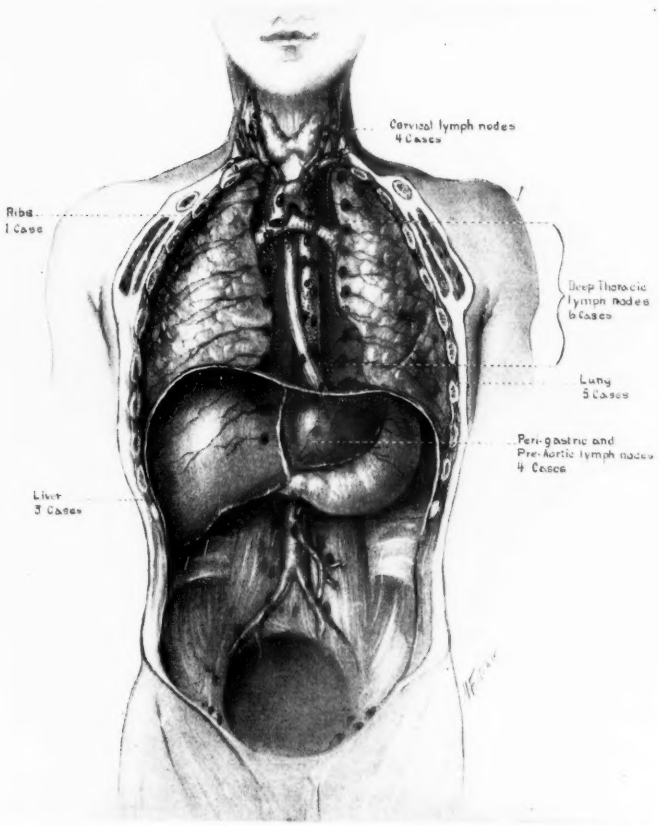

Fig. 7. Diagrammatic sketch illustrating the relative frequency with which the various organs and lymph node areas are involved in secondary deposits from carcinoma of the œsophagus. The diagram is based on 27 postmortem examinations. Of this number 13 cases showed no evidence of metastases.

TREATMENT

Treatment by radical surgery. Surgical approach to either end of the œsophagus is readily accomplished and various successful procedures have been developed for radical removal of new-growths in these locations. In the cervical region the affected portion of œsophagus is excised and a new tube is fashioned from a transverse skin flap. The operative mortality following this procedure is not high. Turner reports 9 cases operated upon with no mortality and a length of life after operation of 3 months, 4 months, 6 months, 1 year, 14 months, and 18 months. At the time the report was made 2 patients were still alive and well; 1, 2 years and the other 9 years after operation. Turner found the length of life was only 4 months in the untreated cases.

The abdominal portion of the œsophagus may be approached by abdominal route and also by a posterior mediastinotomy (Lilienthal). The operative mortality and the end-results of a series of cases treated by these procedures does not appear in the literature and one suspects that the results are not satisfactory.

Torek, in 1913, reported the first successful case of resection of the thoracic portion of the œsophagus for carcinoma. He obtained a

TABLE III.—METHOD OF TREATMENT

The number of cases treated by the different methods and the average length of life is shown. Patients treated only by gastrostomy were those in which the general condition was too poor to permit palliative radiation

		Cases	Average length of life after admission (in months)
External irradiation only	Moderate	12	5.33
	Inadequate	18	3.39
Intra-œsophageal irradiation only	Radium in capsules	11	4.04
	Radon seeds	1	1.0
External plus intra-œsophageal irradiation	Radium in capsules	3	4.67
	Radium in capsules and radon seeds	1	6.0
	Radon seeds	1	1.0
Gastrostomy only		22	3.31
Gastrostomy plus external irradiation		71	6.27
Gastrostomy plus intra-œsophageal irradiation	Radium in capsules	19	3.68
	Radon seeds	1	6.0
Gastrostomy plus external and intra-œsophageal irradiation	Radium in capsules	9	3.39
	Radium in capsules and radon seeds	2	15.5
	Radon seeds	0	
No treatment or non-specific treatment		10	3.1

cure. His patient died 13 years later of pneumonia without recurrence of her cancer. In a later communication, Torek called attention to the difficulties of the operative treatment and outlined the various causes of failure, but concluded that operation offers the only hope of cure. The operative mortality, he believes, can be lowered by careful selection of cases. Saint made a very systematic and impartial review of the surgery so far attempted for carcinoma of the œsophagus. He concluded that the anatomical structure and relationships of the œsophagus, the highly malignant nature of the disease, the frequency of metastases, and the danger of fatal postoperative shock and infection should lead to the use of palliative measures as a routine.

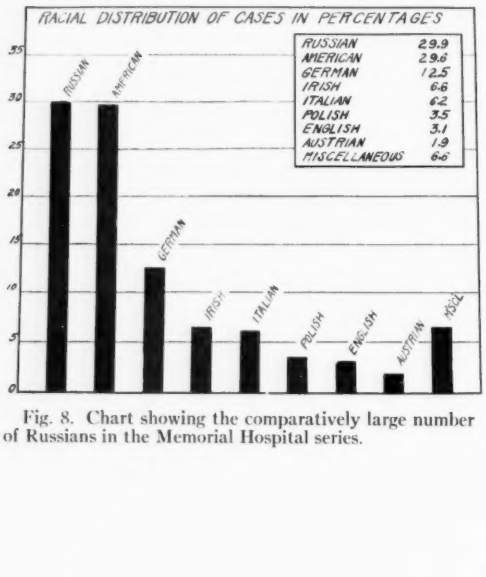

Fig. 8. Chart showing the comparatively large number of Russians in the Memorial Hospital series.

Treatment by irradiation. External irradiation by means of X-ray and radium has in the past been given merely with the hope of retarding the tumor growth and perhaps lessening the severe pain often associated with the late stages of the disease. The dosage has been totally inadequate to cause complete regression. From a review of the anatomy and pathology of carcinoma of the œsophagus, it appears logical to expect more from roentgen radiation of these lesions. With this in mind we are at present using a method of accurately outlining on the skin surface four treatment portals so located that the beams of X-ray will crossfire at the level of the tumor. The beam of radiation is so directed as to pass through the least possible amount of lung tissue. It has been found that 2,000 r may be given through each of four portals without blistering the skin or causing severe constitutional symptoms. This technique is being

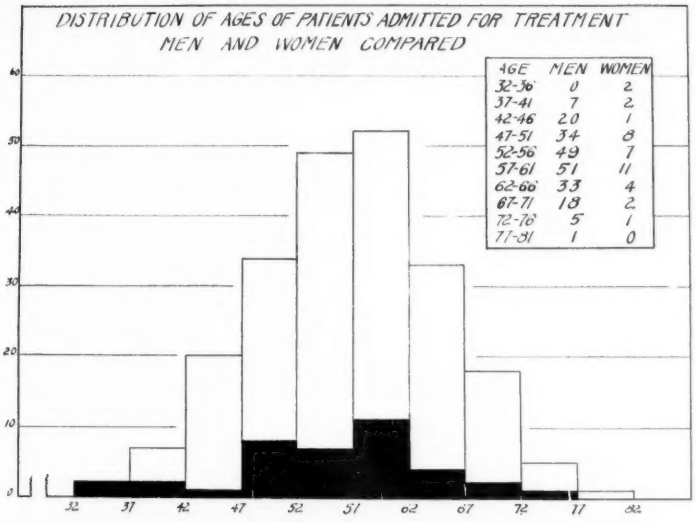

Fig. 9. Chart showing the comparative age distribution in carcinoma of the œsophagus. The women are represented by the solid black portions. The female sex tends to acquire carcinoma of the œsophagus at an earlier age than does the male.

used in a series of cases and the results will be reported at a later date.

Intra-œsophageal irradiation by means of radium in the form of capsules has been used by Guisez in a large number of cases. He reports temporary, but definite decrease in dysphagia in all his cases and his results are surprisingly good. He reports 270 patients treated with intra-œsophageal radium; 30 patients lived more than 18 months, 4 died of intercurrent affections without any evidence of cancer in the œsophagus; 1 was alive 10 years; 1, 11 years; 1, 5 years; 4, 4 years; 4, 3 years; and 12 more than 18 months without evidence of disease. In all these cases biopsies were positive. He uses radium tubes of Dominici arranged in tandem and held in a bougie by means of which the tubes are accurately placed in relation to the tumor. Two or three tubes with a total of 10 to 12 centigrams of radium bromide screened by 1.5 millimeters of platinum are used and inserted every 2 days for 10 to 12 hours. Five or six treatments are usually given. Of the cases which we have treated by intra-œsophageal irradiation, none has lived long enough to encourage us to continue with this method.

The insertion of gold filtered radium emanation seeds directly into the tumor has given only indifferent results (Table III).

Intra-œsophageal manipulations. Bougienage and dilatation of the carcinomatous stricture has been given a trial at the Memorial Hospital. The deliberate tearing and stretching of a carcinomatous stricture with the resultant opening of new blood and lymph channels for dissemination of disease together with the danger of rupture of the œsophagus, hæmorrhage, and fatal sepsis have led us to limit the number of cases treated by this method. During the later stages of the disease it becomes impossible to dilate the lumen and a gastrostomy becomes necessary unless one elects to send the patient home to die slowly of starvation.

None of the cases in our series was intubated or treated by coagulation with the high frequency current. These methods are occasionally advocated in the literature.

Palliative treatment. Gastrostomy if done early in the course of the disease should have practically no operative mortality. If this procedure is carried out in every case regardless of the stage of the disease, a certain num-

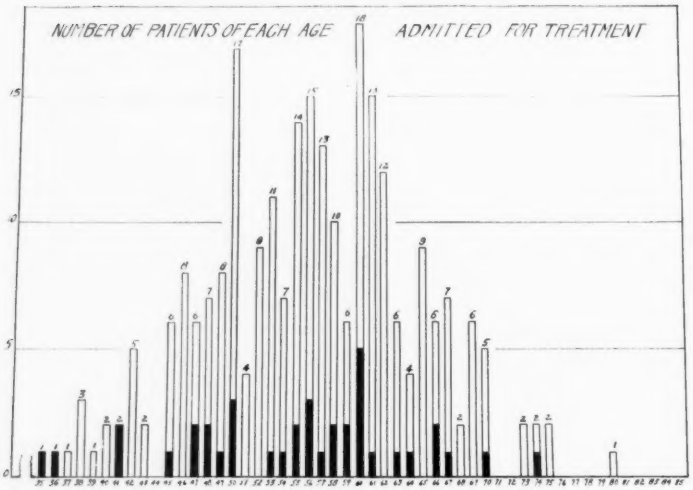

Fig. 10. Chart showing the number of cases of each age. The youngest patient in this series was a woman 35 years of age, and the eldest was a man of 80. More cases, male and female, acquired the disease during their sixtieth year than during any other similar period of time. The females are represented by the solid black.

ber of cases will die after operation, but the causes of death will usually be due to perforation into the aorta with fatal hæmorrhage, pneumonia from a broncho-œsophageal fistula (Fig. 12), mediastinitis, etc. Such must be called postoperative deaths, but they are in reality deaths due to the patient's disease. In most cases the operation is done under novocain infiltration and block anæsthesia and is accomplished without shock to the patient who sits up in bed on return to the ward and is fed through his gastrostomy tube immediately. He is out of bed on the third day after operation and soon begins to gain weight. The dysphagia definitely decreases and the patient's morale improves with his strength. Our recent results with gastrostomy are very encouraging and these statistics together with a description of the operative technique have been published (Martin and Waston).

At Memorial Hospital palliation has been aimed at and gastrostomy is usually done unless contra-indicated or refused by the patient. This procedure has been combined with external or intra-œsophageal irradiation and in some cases with both. Seventy-one patients having had gastrostomy and external irradiation lived an average of 6.27 months after treatment. Twelve patients treated by moderate doses of external radiation lived an average of 5.33 months after treatment. Table III shows the number of patients treated by various methods and the results.

PROPHYLAXIS

We do not see cancer of the œsophagus in patients with sound, healthy, clean, teeth. Oral sepsis is usually advanced or, if the patient be edentulous, it is possible to obtain a history of preceding dental caries in most cases. It seems to be a frequent disease among the Russian poor who take very little care of their teeth. Prophylaxis should begin with care of the teeth. Alcohol, hot fluids, excessive use of tobacco, and spiced food should be eliminated. Slow and complete mastication of food would prevent œsophageal trauma. Patients with œsophageal spasm must be treated and the public educated to the possible seriousness of such trifling symptoms as a feeling of substernal pressure and temporary dysphagia.

PROGNOSIS

Carcinoma of the œsophagus is a rapidly fatal disease. The average length of life from

Fig. 11. Carcinoma of the œsophagus showing the detail which may be brought on by careful radiographic technique.

Fig. 12. Roentgenogram on admission showing a broncho-œsophageal fistula developing in a carcinoma of the œsophagus. This patient had a gastrostomy performed for feeding purposes and improved enough to return home in 2 weeks after operation.

the onset of symptoms in this series was 10½ months and the average length of life after application to the hospital was 4.83 months in the 208 cases followed. The disease advances so swiftly when symptoms are present that a fatal termination occurs often before metastases are demonstrable at autopsy. The disease spreads by three methods: direct extension, lymphatic permeation, and the blood stream. At one time it was thought that the small islands of new-growth sometimes seen dotted about the mucous membrane some distance from the primary lesion were carcinoma implants. Since then it has been shown, however, that these were really upshots to the surface of permeated intramural lymphatic vessels. Table IV gives the average length of life in the different groups.

Of the thousands of cases of carcinoma treated yearly, there has been a salvage of not more than 10 cases. The lethal nature of the disease becomes increasingly important when we realize that from 3 to 4 per cent of all cancer deaths occur in patients with carcinoma of the œsophagus. The high mortality and the relative frequency of the disease make worth while the studying in detail of any large series of cases, with the hope that some clue to an earlier diagnosis may be obtained or a more rational method of treatment suggested. A

TABLE IV.—AVERAGE LENGTH OF LIFE IN EACH GROUP

Epidermoid carcinoma	Grade 1	Grade 2	Grade 3	Adenocarcinoma	Transitional cell
Cases with complete data	10	118	29	13	5
Average length of life from onset of symptoms (in months)	6.34	8.27	12.22	18.68	14.6
Average length of life after admission to hospital (in months)	2.60	4.56	4.5	7.73	8.7
Average length of life after operation (in months)	2.55	3.74	5.88	10.5	7.1

mortality of practically 100 per cent seems a hopeless situation and small recompense for the time and effort which has gone into the investigation of this disease. It seems wise to attempt a cure only in the very few favorable cases and to treat the remainder in a routine palliative fashion—possibly best by external irradiation combined with gastrostomy.

SUMMARY

1. Intimate knowledge of the anatomy and histology of the œsophagus is essential to the understanding of the treatment problems of cancer in this organ.

2. The exact etiology of œsophageal carcinoma is still obscure, but definite predisposing and exciting factors are known and should be an aid in prophylaxis.

3. Cancer of the œsophagus makes up between 3 and 10 per cent of all the carcinoma deaths.

4. The disease is most frequent in the lower third of the œsophagus.

5. Of the 267 cases with positive biopsies, 15 were grade 1, 148 grade 2, 39 grade 3, 19 adenocarcinoma, 6 transitional cell carcinoma, and in 40 cases the tissue was unsatisfactory for grading.

6. Adenocarcinomata of the œsophagus are more slowly growing and give symptoms earlier than do the squamous cell lesions.

7. Of the cases coming to autopsy 48 per cent showed no evidence of metastases.

8. Bronchopneumonia was a cause of death in 48 per cent of the cases.

9. Radical surgery of the œsophagus is indicated in a few early cases.

10. The routine treatment should be palliative.

11. Gastrostomy followed by external irradiation offers the most satisfactory palliation.

12. Prophylaxis should be stressed.

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DIVERTICULUM OF THE URINARY BLADDER

An Analysis of One Hundred Cases[1]

ADOLPH A. KUTZMANN, A.B., M.D., F.A.C.S., Los Angeles, California
From the Urological Service of the Los Angeles General Hospital

THE status of bladder diverticulum has passed from a rare clinical entity to a common urologic diagnostic finding. It is a far cry since there appeared, in all, but 6 cases in the American literature and when other contemporary reports showed but 6 collected cases from the world's literature in which the sac had been excised. Prior to the present century the occurrence of diverticulum was usually found upon postmortem examination. The ready facility now of its clinical recognition is due to the progress achieved in cystoscopic and roentgen-ray procedures in urologic diagnosis.

Diverticulum of the urinary bladder has led to some interesting anatomicophysiological problems, chief of which have been etiology and anatomy. Various theories have been promulgated and according to these theories diverticula may be divided in four principal groups: (1) diverticula which are caused as a result of congenital and acquired factors; (2) diverticula congenital in origin; (3) diverticula of the acquired type; and (4) diverticula that may be either purely congenital or purely acquired.

Some observers maintain that diverticula are congenital and have based such an opinion on the fact that they occur in infants and young children. Others have contended that all diverticula are acquired since they are rarely found when urinary obstruction is absent. Most of the present day observers take a more logical intermediate viewpoint, namely, that diverticula may be the result of both congenital and acquired factors. They may exist from birth, chiefly those in the fundus, taking origin probably in a patent urachus, while the remainder are secondary to back pressure, such affected bladders probably giving way at their points of congenital weakness. An analysis of the present series of cases leads the writer to the same conclusion since it was possible nearly always to demonstrate some type of bladder neck or urethral obstruction.

Anatomically the walls of the diverticula are essentially composed of fibrotic and connective tissue fibers permeated with inflammatory elements. Some observers have reported the finding of occasional bundles of muscle fibers which when present are said to be widely scattered or interwoven with the fibrous tissue. There is no evidence of any layer formation similar to that found in the bladder wall proper. Usually all diverticula have a smooth glistening lining membrane, unlike the bladder mucosa in appearance and showing histologically a flattened type of epithelium. This has not, however, been substantiated by some observers. Examination of the pathological material from the diverticulectomies in the present series of cases revealed that the diverticula were composed of fibrous tissue with chronic inflammation. A lining epithelial membrane was present in all and appeared histologically to be of a more flattened squamous type than that found in the bladder proper.

Clinically, diverticula of the bladder have presented many interesting facts. There is no distinctive symptomatic syndrome. This lack of symptoms makes their recognition by diagnostic procedures with the cystoscope and X-ray one of importance. At times the presence of diverticula may not be discovered by these urological diagnostic procedures but may later be found at open operation. Significant factors, as situation in relation to position and drainage, size of the orifice and sac, number, exact nature of the etiological obstructing factor, type of urinary infection, must be carefully ascertained. Recognition of such complicating associated factors as calculus, carcinoma, leucoplakia, and tuberculosis are of paramount importance if the condition is to be adequately remedied. Treatment in most cases has been the relieving of the ob-

[1]Read before The California Medical Association, May 9, 1932.

A.

B.

Fig. 1A. Cystogram showing typical vesical diverticula, one large and several smaller ones, associated with a vesical obstruction due to a benign hypertrophy of the prostate. The irregular outline which is to be noted in the remainder of the bladder is due to cellule formation.

Fig. 1B. Drawing demonstrating anatomically the orifice of a true diverticulum into the bladder, shown in the accompanying cystogram.

structing factor. If the diverticulum is of the retention type, urinary stasis occurs which usually leads to severe urinary infection with organisms of the urea-splitting type, as the streptococcus, staphylococcus, or Bacillus proteus. Such an infection may result in a very irritating ammoniacal urine, and therefore such diverticula must also be treated either by resection of the entire sac or a plastic procedure to their orifices so as to insure proper drainage. The latter procedures are also usually applied to large diverticula.

There have been observed 100 cases of bladder diverticulosis in the Los Angeles General Hospital within the last 5 years and for that reason the following analyses and conclusions are detailed.

ANALYTICAL SUMMARY OF ONE HUNDRED CASES OF DIVERTICULA OF THE URINARY BLADDER

During the last 5 years there have been 5,984 admissions to the urological service. Among these have been observed 100 cases of diverticulosis. These cases have been divided into two groups: true diverticula and false or incipient diverticulosis. The basis for this division is upon the criteria that false or incipient diverticula are for the most part cellules or shallow wide mouthed depressions due to the protrusion outward of the epithelial lining between hypertrophied muscle bundles and are nearly always multiple and found throughout the bladder (Fig. 2); the true diverticula are more commonly single and larger in size, exhibiting a definite orifice, having an anatomical sac-like structure, and are usually situated in the region of the ureters (Fig. 1).

There were 72 of the true type and 28 of the false cases. This makes an incidence of 1.2 per cent or one in every 83 general urological admissions. Of the 72 true cases, 43 were found among 467 cases of benign hypertrophy of the prostate or an incidence of 9.1 per cent (1 in 10.8); 14 were among 83 bladder neck contractures and median bars—11.8 per cent (1 in 5.8); 3 were among 254 carcinomata of

A.

Fig. 2A. Cystogram showing a shallow, irregular, and indented bladder outline due to diffuse cellule formation or early (false) diverticulosis.

B.

Fig. 2B. Drawing of anatomical formation of a bladder with early (false) diverticulosis or cellule formation and resulting in a cystographic outline shown in Figure 2A.

the prostate—1.1 per cent (1 in 84); and 3 were among 21 urethral strictures necessitating operation (external urethrotomy)—14.2 per cent (1 in 7) (Table I). It is interesting to note from these figures that the relative incidence is more common among bladder neck contractures, median bar and urethral strictures than in the presence of benign hypertrophy of the prostate.

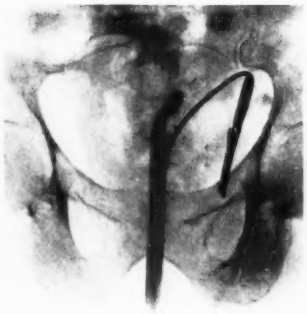
TABLE I.—INCIDENCE—1927–1931

	Number	True diverticulosis	False diverticulosis	True cases	
				Percentage	Ratio
Total urologic admissions	5984	72	28	1.2	1:83
Prostatism Benign hypertrophy	467	43	21	9.1	1:10.8
Contractures Median bars	83	14	4	16.8	1:5.8
Carcinoma	254	3	2	1.1	1:84
Urethral stricture (necessitating operation)	21	3	.....	14.2	1:7

An analysis of the symptoms shows that bladder diverticulum is not a distinct clinical syndrome (Table II). The incidence of various urinary disturbances presents a clinical picture similar to that of an obstructive uropathy in the lower urinary tract (bladder neck and urethra) with a complicating infection. Frequency in 53 cases, difficulty in cases, nocturia in 40 cases, dysuria in cases, dribbling in 27 cases, and burning in 23 cases were the symptoms most frequently encountered. Twenty-one cases entered the hospital with complete retention. The outstanding characteristic of the symptomatology was the

A.

B.



C.

Figs. 3A and B. Diagnostic demonstration of a retention diverticulum by means of the contrast cystographic method utilizing 12½ per cent sodium iodide and air.

Fig. 3C. Illustrating a second cystoroentgenographic method of diagnosis in which an ureteral catheter is coiled up in the diverticulum.

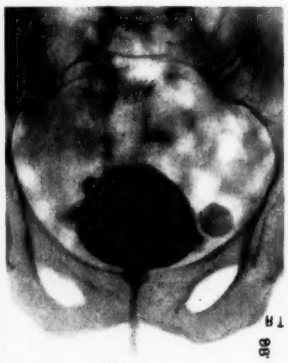


Fig. 4.

Fig. 5.

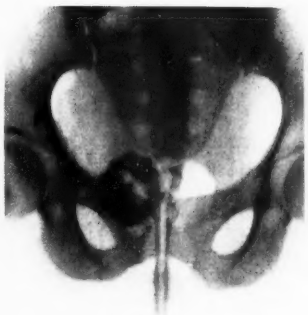


Fig. 6.

Fig. 4. Cystogram showing several definite true diverticula in a woman in whom the only obstructing factor that could be demonstrated was an hypertrophied bladder trigone.

Fig. 5. Cystogram illustrating one large diverticulum and a diffuse early diverticulosis in a man with a spinal cord injury.

Fig. 6. A contrast air cystogram in a woman. The retained sodium iodide is held in a pericystic abscess connecting directly with the bladder and not in a diverticulum.

long duration, some patients having had urinary disturbances, in a mild form, well on to 15 years.

A distribution of 97 cases in men and 3 in women emphasizes the fact that diverticulum of the bladder is a disease of the male urinary bladder. Most cases were found in later life, 91 per cent occurring after the age of 50 years; the largest number in any one period was 42 and occurred in the seventh decade of life. No infants nor children were encountered (Table III). This distribution can be assumed as supporting the "acquired theory," showing that it is necessary first that an obstructive process develop.

True diverticula of the bladder tend toward singularity; for instance, 38 cases had 1 diverticulum, 21 cases had 2, and 12 cases had 3 or 4. This distribution of the diverticula was essentially in the ureteral region, as evidenced by the fact that in 24 cases the opening was in the right ureteral region, in 13 in the left ureteral region, in 22 the openings were bilateral, and in 7 in the posterior and fundal

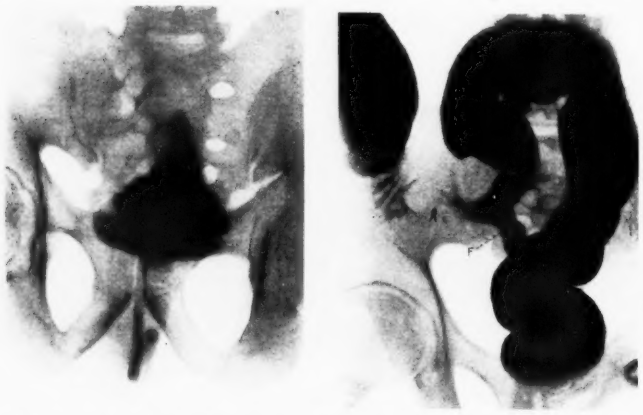


Fig. 7A, left. Cystogram illustrating an opening in the fundus of the bladder caused by a perforating intestinal carcinoma. Such a picture may be confused with a diverticulum.

Fig. 7B. Roentgenographic visualization of the intestinal tract of the same case. The obliterated portion *A* is the site of the growth while *F* is the course of the fistula connecting with the bladder.

areas (Table IV). A total of 65 of the 72 true cases (90 per cent) were found in the region of the ureters and this fact can be taken as further confirmatory evidence that the weakest points in the bladder musculature are in the vicinity of the ureteral orifices; or that there may remain from a faulty embryological development small patent ureteral buds which in later life develop into diverticula, a fact that must be considered in some cases in women in whom examination fails to disclose any obstructing factor. This may be explained by the embryological development of the ureter as it buds off the cloaca, or by the fact that there can occur an absence of longitudinal muscle at these points. It may therefore be considered that a bladder wall must possess congenitally weak areas as the site of election for diverticulum formation, but that a diverticulum may never occur in the male unless there is an obstructive factor at either the

TABLE II.—SYMPTOMATOLOGY

	Cases
Frequency	53
Difficulty	44
Nocturia	40
Dysuria	29
Dribbling	27
Burning	23
Retention	21
Hæmaturia	12
Urgency	10
Hesitancy	6
Backache	5
Epididymitis	2
Tenesmus	1
Chills and fever	1
Loss of weight	1
Weakness	1
Suprapubic pain	1
Pain in right flank	1
Suprapubic sinus	1

TABLE III.—AGE

Years	Cases
0–10	0
11–20	0
21–30	2
31–40	3
41–50	4
51–60*	14
61–70*	42
71–80*	25
81–90*	10
Total	100

*91 cases (91 per cent) within prostatic age.

TABLE IV.—LOCATION*

	Cases
Right ureteral region	24
Left ureteral region	13
Bilateral	22
Right ureteral and fundus	4
Left ureteral and fundus	1
Bilateral and fundus	1
Fundus and posterior	7
Generalized or incipient diverticulosis	28
Total	100

*65 of 72 true cases (90 per cent) in region of ureters.

A. B. C.

Fig. 8. Cystograms showing various bladder deformities associated with diverticula of the male urinary bladder. A, Hour-glass deformity. B, Illustrates an elongation of the fundus with multiple diverticula. C, Fixed fundus resulting in a broad outline.

bladder neck or in the urethra. Such bladders as have no congenitally weak areas may in the presence of a urinary obstruction give rise to only a diffuse formation of deep trabeculations or cellules (grouped in this series as incipient diverticulosis).

In most cases there was residual urine, 7 patients having 50 cubic centimeters or less, 19 between 50 and 100 cubic centimeters, 16 cases 100 to 200 cubic centimeters, and 23 over 200 cubic centimeters; in 21 patients there was complete retention.

TABLE V.—ETIOLOGICAL CONDITIONS

Condition	True cases	False cases	Total Cases
Prostatism Hypertrophy, contracture	43	21	64*
Median bar	14	4	18*
Carcinoma	3	2	5*
Urethral stricture	3	0	3*
Carcinoma of bladder	2	0	2
Cord injury	1	0	1
Spastic paraplegia	0	1	1
Urethral caruncle (female)	1	0	1
Hypertrophied trigone (female)	1	0	1
Unknown	1	0	1
Not stated (1 female)	3	0	3
Total	72	28	100

*Total, 90 per cent of cases.

TABLE VI.—ASSOCIATED CONDITIONS

	Cases
Calculi	
Bladder (Including 5 cases with calculi in diverticulum)	12
Upper urinary tract	3
Prostatic	1
Total calculi	16
Lues	7
Bladder tumors (carcinoma)	2
Papillary carcinoma of intestine invading bladder	1
Epithelioma of kidney pelvis	1
Adenocarcinoma of rectum	1
Epithelioma of ear	1
Diabetes	1
Total	30

TABLE VII.—TREATMENT

		Cases
To etiologic condition:		
Prostatectomy	One stage suprapubic	2
	Two stage suprapubic	38
	Perineal	4
Total		44
Punch	Open	11
	Closed	4
Total		15
Cystotomy		15
Prostatic resection		1
Grand Total		75
To diverticula:		
Diverticulectomy		8
Squier operation		3
Punching orifice		3
Percy cautery		3
Total		17
No treatment		18
Refused treatment		3

A. B.

C. D.

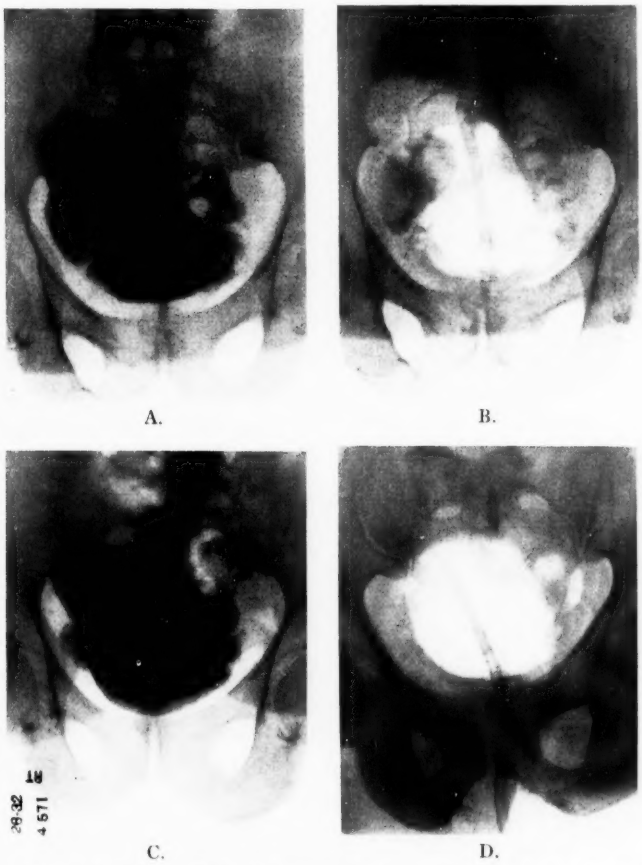
Figs. 9A and B. Contrast cystograms showing two retention diverticula on the posterior wall of the bladder.

Figs. 9C and D. Contrast cystograms several months after diverticulectomy demonstrating a good anatomical result.

An analysis of the etiological conditions showed that prostatism and urethral stricture, especially the former, were the dominant productive factors in 90 male patients. There were 64 cases of benign hypertrophy with 43 cases of true diverticula; 18 cases of bladder neck contracture and median bar formation with 14 cases of true diverticula; 5 cases of prostatic carcinoma with 3 true cases; 3 cases of urethral stricture with true diverticula; the remainder were individual cases of urethral caruncle (female), hypertrophied trigone (female), bladder carcinoma, cord injury, spastic paraplegia, and 3 cases (1 female) not stated (Table V).

In 30 cases there were associated conditions. Sixteen exhibited urinary calculi distributed as follows: 12 with vesical calculi, 5 of which were within the diverticulum; 3 with renal calculi; and 1 with prostatic calculi. Seven patients had lues, 2 had carcinoma of the bladder, and 1 each had an epithelioma of the kidney pelvis, adenocarcinoma of the rectum, epithelioma of the ear, a papillary carcinoma of the intestine invading the bladder and diabetes (Table VI). In none of the cases of diverticula was there found an associated neoplasm, leucoplakia, or tuberculosis.

Treatment was directed chiefly toward the etiological condition and secondarily to the



Figs. 10A and B. Contrast cystograms demonstrating a large retention diverticulum in the right wall of the bladder. There are several smaller diverticula on the left wall but these drain well.

Figs. 10C and D. Contrast cystograms 14 months after treatment with the Percy cautery to the diverticulum and its orifice. Although there has been a slight change in actual size, satisfactory drainage has been achieved.

diverticulum if it was of the retention or large type. Upon this basis the etiological condition was corrected or treated palliatively in 75 cases and the diverticulum was treated directly in 17 cases. In 44 cases prostatectomy was done (2 in one stage, 38 in two stages, and 4 by the perineal route); in 15 cases bladder neck punch operations were done (11 open and 4 closed); in 15, cystotomy was done; and in 1 a prostatic resection with the high frequency loop. In the 17 cases in which the diverticulum was treated directly, the following operations were done: diverticulectomy, 8 cases; the Squier operation, 3 cases; orifices punched out, 3 cases; Percy cautery, 3 cases (Table VII).

A study of the follow-up letters has shown that our method of treatment was adequate in the majority of operative cases. Most cases showed improvement as evidenced by a marked diminution in symptoms and urinary infection, disappearance of residual urine, and distinct gain in general health. Follow-up cysto-urographic studies of such treated cases

as could be reached who had had a prostatectomy or had had in addition some plastic work on the diverticulum orifice, revealed for the most part very little change in the size of the diverticulum proper. However, the important factor—drainage—had been achieved. An excellent anatomical result was obtained in the several patients who had had a diverticulectomy. From our data it may be inferred that a minimum amount of attention may be paid to the diverticulum proper but that it is most important to remove all etiological obstructing factors and to institute thorough drainage. If such has been achieved and there are no diverticula of the retention type present, the patient will be greatly benefited.

Unless the indications be definite, such as retention, poor drainage, marked infection, small orifices, diverticula for the most part can be ignored following the remedying of the bladder neck obstruction. Attempts to treat surgically some types of diverticula, as for instance those situated in the subtrigonal and ureteral regions may lead to much additional technical difficulty, often producing surgical shock and even death.

CONCLUSIONS

1. Diverticulum of the urinary bladder is a disease which affects the male chiefly and occurs for the most part in later life during the prostatic age. It is nearly always associated with an obstructive condition as prostatism or urethral stricture.

2. The incidence of diverticulum is as follows: in the urologic cases in general, 1 per cent; in benign hypertrophies, 9.1 per cent; in contractures and median bar obstruction, 16.8 per cent; in urethral strictures necessitating operation, 14.3 per cent; and in carcinoma of the prostate 1.1 per cent. No definite clinical symptomatology is noted except possibly, if a lower urinary tract obstruction with infection is present, there is an accentuation of the characteristic symptoms of the associated condition.

3. Diverticulum of the urinary bladder is the result of both congenital and acquired anatomical factors.

4. Anatomically it was found in the present series that the walls of the diverticulum showed fibrous tissue with permeation of chronic inflammatory elements. The diverticula were lined with smooth, glistening membrane; histologically, the flattened type of epithelium.

5. Diverticulum of the urinary bladder is treated most satisfactorily by the correction of the obstructing factors, only such diverticula being individually treated as may be of the retention type, or of a large size. This method of procedure will give gratifying relief from symptoms that have been intense and of long duration.

HYPERTROPHIC INTESTINAL TUBERCULOSIS[1]

A. A. DAVIS, CH.M. (VICT.), F.R.C.S. (ENG.), MANCHESTER, ENGLAND
Surgical Registrar, Manchester Royal Infirmary

THE present paper is based upon a review of twenty-nine cases of hypertrophic tuberculosis of the intestine treated in the Surgical units of the Manchester Royal Infirmary during the past ten years. The number of cases recorded is small, the disease being a comparatively rare one (during the same period, and in the same institution, the number of patients admitted suffering from intestinal carcinoma was 1123). The results of surgical intervention, however, particularly when of a conservative nature, have been so generally successful in this group of cases, that it is suggested that a statistical consideration of the etiology and treatment of the disease based upon them might be of value.

It is perhaps advisable to indicate at the outset that consideration is limited entirely to those cases corresponding to Type 4 of the so-called "French" classification of intestinal tuberculosis. This, which is purely a pathological one, enumerates the following varieties: (1) the ulcerating type, or tuberculous enteritis, (2) the stenosing type, (3) the enteroperitoneal type, and (4) the hypertrophic type.

Types 1 and 2 being invariably secondary to phthisis in adults, and forming the bulk of intestinal cases in children, constitute the overwhelming majority of all cases of intestinal tuberculosis. The remaining types are comparatively rare, but as one of these, the last, is the only variety amenable to surgical treatment—with the exception of those secondary cases in which perforation or acute obstruction demand urgent relief—it is only this type which is seen with any degree of frequency by the surgeon.[2] This is illustrated by the fact that of the 35 cases of all types of intestinal tuberculosis treated in the surgical wards of the Royal Infirmary during the period under review, 29 were of the true hypertrophic variety.

[2]The extensive operative procedures advocated by Archibald, of Montreal, for uncomplicated secondary tuberculous enteritis have never been widely adopted, in spite of the good results claimed by this author-ity.

A comparative analysis of these cases follows.

ETIOLOGY

Situation. The situation of the focus of disease is indicated in Table I.

TABLE I.—DISTRIBUTION OF THE LESIONS

	Cases
Ileocæcal region	22
Sigmoid colon	3
Hepatic flexure	1
Ascending colon	1
Appendix	1
Jejunum	1
Total	29

These figures correspond fairly closely to the majority of published surgical data. Of Mummery's list of 100 collected cases of hyperplastic tuberculosis affecting the colon, 87 involved the cæcal region, 6 were confined to the sigmoid, while the whole or a large part of the colon was invaded in the remaining 7. Anderson and Munro, reporting 9 similar cases, state that 6 were of the cæcal type, 2 were situated in the transverse colon, while 1 was of the diffuse type involving the ascending and transverse limbs. No cases involving the transverse colon occurred in the Infirmary series. It is a rare lesion, only 2 of 43 cases of hyperplastic intestinal tuberculosis reported by Caird being affected in this region. Similarly I have been unable to find in our series an example of the peculiar "gas-pipe" colon, where the whole colon is the seat of a generalized tuberculous thickening, but this is scarcely surprising, as the type is extremely rare, the only published cases being single ones reported by Briddon, Lartigau, Elliott, and Mummery.

Age incidence. The average age of the patients was 30 years, the youngest being 9, the oldest 69 years.

These figures correspond closely to similar published statistics. The average age in Mummery's 80 cases was 32 years, the oldest patient being 78 years, and the youngest 7. Erdman's 6 cases gave an average age of 30

[1]Presented before the Manchester Surgical Society, March, 1932.

Fig. 1. Hypertrophic ileocæcal tuberculosis. Case No. S.1266/29. J. G., male, aged 68 years. Symptoms of chronic intestinal obstruction for 6 months, with a large fixed tumor in the right iliac fossa. Operation, November 20, 1929, ileotransverse colostomy (tumor irremovable). Examined November 12, 1931, and found fit and well. He has gained one stone in weight, has no intestinal symptoms. No tumor is palpable. (Postoperative barium enema X-ray refused.) (X-ray by Drs. Paterson, Twining, and Gray.)

years. Very similar figures are reported by Vikoljski, Mueller, Shiota, and Kuettner. It is of interest to note that this average age of 30 years is also the average age of several large series of phthisical patients.

Sex incidence. Twenty-one of the cases were females, and 8 males.

This sex incidence is somewhat different from that usually accepted, namely, that the sexes are affected with equal frequency. This ratio is illustrated by the list of published figures quoted by Mummery (Table II).

TABLE II.—SEX INCIDENCE

	Cases	Males	Females
Mummery	80	47	33
Conrath	77	36	41
Bernay	71	40	31

Mueller actually reverses the order by stating that males are affected more than females in the proportion of 3 to 2. The discrepancy, one supposes, is due more to the (comparatively) small number of cases reviewed than to any etiological factor.

Incidence of tuberculosis elsewhere. Table III is self explanatory.

TABLE III.—INCIDENCE OF CONCURRENT TUBERCULOUS LESIONS

	Cases
Phthisis	2
Jejunal ulcer	1
Hyperplastic tuberculosis of rectum	1
Tuberculous arthritis of elbow joint	1
Tuberculous ischiorectal abscess and tuberculous stricture of ileum	1
	6
Percentage	20

It will be seen that only 2 of the patients suffered from phthisis—(one may add in parenthesis that now both these patients are free from active disease)—while 3 others had coincident tuberculosis of some part of the gastrointestinal tract. These findings are in accord with the generally accepted view that the disease is not usually associated with tuberculosis elsewhere, except in a small, though definite, proportion of cases. It is interesting to note that the percentage of cases free from other tuberculous disease in Mummery's series, namely 24 per cent, is very close to the figure of 20 per cent in the Infirmary group. (Four of Erdman's 6 cases had quiescent phthisis, but it would appear unjustifiable to accept percentages based on such a small figure.)

The question of primary or secondary infection. These results throw little light on the interminable discussion as to whether hypertrophic intestinal tuberculosis is truly a primary or a secondary disease. Cumston believes that it is "almost always" primary; Hemmeter, that it is usually secondary to phthisis; and all variations of opinion between these two extremes have been registered by various authorities. A variety of causes would appear to account for these differences. In the first place, it is probable that too much importance has been attached to the 2 classical cases of Lartigau and Beck, in which each observer failed to find any evidence of tuberculosis elsewhere, in spite of a most exhaustive and minute postmortem examination. It is surely an exaggeration to make these isolated findings the basis of a contention that *all* the cases are primary in origin. Second, assumptions based on the review of a small number of cases, with consequent misuse of the percentage system, must inevitably lead to many fallacies. In the third place, most of the

TABLE IV.—DURATION OF SYMPTOMS

Average duration	20 months
Shortest duration	3 days
Longest duration	10 years

TABLE V.—INCIDENCE OF INDIVIDUAL SYMPTOMS

	Cases
Alternating constipation and diarrhœa	6
Constipation only	15
Diarrhœa only	4
Bowels regular	3
Blood in stools	2
Slime in stools	3
Blood and slime in stools	3

Palpable mass present in 18 cases (65 per cent).

TABLE VI.—SYMPTOM SYNDROMES

	Cases
Syndrome of chronic intestinal obstruction	15
Syndrome of chronic intestinal obstruction with alternating constipation and diarrhœa	6
Syndrome of acute intestinal obstruction	1
Syndrome of recurrent appendicitis	4
Syndrome of acute appendicitis	3
	29

larger series include in the figure all the widely varying types of intestinal tuberculosis, in spite of the fact that (at least in adults), the very common ulcerative type is almost invariably secondary. In this connection some figures quoted by Lawrason Brown and Sampson are of interest. On postmortem examination Heller found primary intestinal tuberculosis in 16 of 107 cases (in children in whom the incidence of the primary type is admittedly most common); Bonome in 126 cases out of 769 cases of tuberculosis; Biedert in 16 out of 3104 cases of tuberculosis; Bovaird in 150 out of 1481 tuberculous cases; while Gant, in a collected series of 22,725 autopsies, found primary intestinal tuberculosis present in 7.22 per cent. Hartmann goes so far as to state that 85 per cent of all cases of tuberculosis of the intestine in adults is of the hyperplastic type.

Careful assessment of most of the published figures of postmortem, clinical, and X-ray findings suggest that roughly 70 per cent of all cases of hypertrophic intestinal tuberculosis are truly primary in origin. It will be noticed that both in Mummery's and the Royal Infirmary series this figure is closely approximated.

Fig. 2. Hypertrophic tuberculosis of hepatic flexure. Case No. S. 833/24. J. W., male, aged 45 years. Three months' history of subacute intestinal obstruction. Loss of weight very marked. Large fixed tumor in right hypochondrium. Operation, September 22, 1924; ascending transverse colocolostomy (tumor irremovable). Examined November 12, 1931, and found to be in excellent health. Weight steady. No intestinal symptoms. (Postoperative barium-enema X-ray refused). (X-ray by Drs. Paterson, Twining, and Gray.)

SYMPTOMS

The duration of symptoms, the incidence of individual symptoms, and the types of symptom complex, are summarized in the Tables IV, V, VI.

It will be noticed that of the various symptom complexes exhibited, the commonest is that of a subacute intestinal obstruction, with intermittent attacks of intestinal colic, a definite tendency to constipation with very occasional attacks of diarrhœa, the whole extending over a fairly lengthy period of a year or more. Alternating constipation and diarrhœa, the presence of blood or slime in the stools, or diarrhœa alone, are only very occasional symptoms, but a striking feature is the presence in 65 per cent of the cases of a palpable abdominal tumor noticed in more than half that number, by the patient himself. In one case acute intestinal obstruction, a complication of comparative rarity, supervened. The

Fig. 3. Hypertrophic tuberculosis of hepatic flexure and first part of transverse colon. (Seen too late for statistical inclusion.) Case No. S. 1226/30. J. T., male, aged 65 years. Fifteen months' history of chronic intestinal obstruction, lately becoming subacute. Large tender fixed mass in right hypochondrium. Operation, October 16, 1930, ileo-transverse-colostomy (tumor irremovable). Examined November 12, 1931. Health good; entirely free from symptoms. Considerable increase in weight. (Post-operative barium-enema X-ray refused.) (X-ray by Drs Paterson, Twining, and Gray.)

frequent vomiting which Miles says is occasionally present did not appear in our series.

Four of the case histories closely simulated that of recurrent appendicitis, with occasional attacks of moderately severe pain and tenderness in the right iliac fossa and a corresponding slight rise in temperature. These symptoms were probably the result of a superveningperityphilitis of colon bacillus origin, rather than of an acute tuberculous exacerbation.

The most interesting cases, however, from a symptomatic point of view, were those which so closely simulated a typical acute non-specific appendicitis as to be indistinguishable from it. It should be stated at once that this type is not the same as the so called "tuberculous appendicitis," in which the diagnosis is made only by microscopic examination of an appendix removed for the ordinary non-specific inflammation. In each case, typical moderately advanced ileocæcal tuberculosis was found at operation, and verified histologically later. It would appear that the symptomatology in these cases is the result of an acute colon bacillus infection involving an appendix, the resistance of which has been crippled by long standing lymph and bowel stasis of tuberculous origin.

It should, however, be borne in mind that a considerable number of cases of non-specific acute appendicitis present, at operation, a cæcum so infiltrated and thickened that a tentative diagnosis of ileocæcal tuberculosis is made at the time, and further operative procedures planned for the future. While it is undoubtedly true that most surgeons of experience rarely find the diagnosis in these cases a matter of difficulty, more frequent biopsies would be of considerable practical and scientific value. In one case in which this procedure was adopted, no evidence of tuberculosis was found, and the patient continues in perfect health. Five similar cases, all of which were labelled as tubercle, but in which no biopsy was performed, remain in perfect health, with no sign of the fistula which inevitably follows appendicectomy alone in the presence of cæcal tuberculosis. It is possible that a good deal of misapprehension has resulted from this diagnostic difficulty, leading to the occasional employment of unnecessary operative procedures.

It is interesting to note that of Eisendrath's 52 cases, 16, or 25 per cent, had symptoms identical with those of acute appendicitis.

PATHOGENESIS

Some authorities consider that the appendix provides the initial starting point in the disease, providing a parallel with the extremely frequent tendency of that organ to acute infection. Kelly and Hurdon, in support of this thesis, state that the appendix usually contains the most advanced lesion while Lynch quotes 5 cases operated upon by him in each of which exposure revealed an appendix standing out "like a badly infected granulating finger" from an apparently healthy cæcum. These statements are easily countered by the frequency of exactly opposite findings, in which the appendix alone remains comparatively unaffected in the midst of the most

advanced surrounding disease, and statistical study suggests strongly that the appendix is primarily involved in not more than 20 per cent of cases. This figure, combined with pathological and clinical findings, helps decisively to refute the statement occasionally made that appendicectomy alone is curative in early cases of ileocæcal tuberculosis, and explains the frequency of fæcal fistula resulting from this procedure.

It is not proposed to enter here into a discussion concerning the entry of the bacillus into the intestinal tissues, whether lymphatic, intestinal, or hæmatogenous, but mention should be made of the statement by Weber and Tante, that they discovered bacilli of the bovine variety in 25 of 28 cases of primary intestinal tuberculosis.

TREATMENT

The methods of operative treatment adopted, together with its incidence and mortality, are shown in Table VII.

TABLE VII.—TYPE AND MORTALITY OF OPERATION

	Cases	Mortality
1. Ileocolostomy alone	17	nil
2. Resection plus ileocolostomy	5	1 case
3. Colocolostomy	1	nil
4. Mikulicz's operation	2	nil
5. Appendicectomy alone	1	nil
6. Laparotomy	3	nil
	29	1 case

It will be noticed that radical removal of the disease was practiced in only 7 cases, the condition being so advanced in the remaining 22 as to be considered irremovable. In these latter, a short-circuit was established as a palliative measure where possible, the lesser procedures being adopted where the patient's condition disallowed any manipulation. The single death which occurred followed resection and ileo transverse colostomy, and was due to a very virulent peritonitis supervening 24 hours after operation. These figures are worth comparing with those of Mummery as set out in Table VIII which is copied from his book. (In these figures are included all of the cases of hypertrophic tuberculosis of the large bowel.)

TABLE VIII.—MUMMERY'S CASES[1]

Operation	Cases	Recovered	Died	Mortality per cent
Resection	63	47	16	25.4
Short-circuiting	16	13	3	18.7
Exclusion with colostomy	7	1	6	85
Exclusion with lateral anastomosis	3	1	2	66
Totals	89	62	27	—

[1] Treated prior to 1910.

Nine similar cases reported by Anderson and Munro all recovered from operation. Resection was performed in 7 cases, ileocolostomy alone in one, and appendicectomy only in the last.

END-RESULTS

Twenty patients only could be traced; the results in their cases are summarized in Table IX. Of the 3 deaths, one occurred 5 months after operation from inanition, one 10 months after from phthisis, and one 5 years later from tuberculous meningitis.

TABLE IX.—ANALYSIS OF END-RESULTS—20 CASES

Average duration since operation	4 years
Free from symptoms	[1]14 cases
Improved	3 cases
Died since	3 cases

[1] In 12 of these cases lateral anastomosis alone had been performed.

These figures provide an interesting commentary on the almost universally accepted opinion that resection is the operation of preference in hypertrophic intestinal tuberculosis. It is, of course, probable that this procedure is productive of slightly better results than those of short-circuiting operations alone—all 7 cases treated radically by Anderson and Munro are apparently cured—but it will be noticed that this small improvement is more than offset by the considerably greater mortality accompanying excision. None of the palliative operations in the Infirmary series were performed where excision was possible, but their results are extremely gratifying. It is of interest, in this connection, to note a comment made by W. J. Mayo in a personal

TABLE X.—WARWICK STATISTICS

Observer	Cases	Number affected by tuberculosis	Percentage
Montreal General Hospital	1,259	20	1.6
Allen	80	2	2.5
Litz	257	8	3
Robson	300	5	1.7
Letule	300	2	.7
Univ. of Pennsylvania	310	6	2
Deaver	7,610	16	.2
Scott	179	1	.5
Mayo	12,003	71	.5
Warwick	210	2	1
Total	22,508	133	1.3%

communication to Masson. He mentions 7 cases of ileocæcal tuberculosis which were so improved by a first stage lateral anastomosis that further treatment by resection was unnecessary.

The possibility of carcinoma supervening is probably much exaggerated, though there is no doubt that it does exist, as two cases recorded by Herzog testify, but it is so rare that it may be completely discounted as an argument for resection.

PRIMARY APPENDICULAR TUBERCULOSIS

One case confined to the vermiform appendix occurred in our series. The symptoms were those of typical recurrent appendicitis culminating in an acute attack, for which the appendix was removed, and only shown on microscopic examination to be tuberculous. The other organs were apparently normal. The patient, unfortunately, is untraceable.

This subject has been exhaustively reviewed by Warwick, who quotes Scott's collected figures concerning the frequency with which tubercle is encountered in the routine examination of all appendices removed for other conditions, principally acute appendicitis. The list shown in Table X is modified from her paper.

In a series of collected English cases, Lockwood found the percentage affected to be 2. Analysis of the Mayo Clinic figures show a considerable decline in the incidence during the last 2 decades, a change ascribed by W. J. Mayo to the almost universal adoption in America of the clean milk supply.

HYPERTROPHIC TUBERCULOSIS OF THE SMALL INTESTINE

An example of hypertrophic tuberculosis involving the jejunum, 18 inches from the duodenojejunal flexure, occurred in our series. This is an extremely rare condition, so uncommon that I have been able to find no more than 8 cases recorded in the literature. (Masson and McIndoe, Cunningham and Snierson, Garvin, Counsellor, Lartigau.) The patient, a man aged 51, gave a 6 weeks' history of subacute intestinal obstruction, with severe colic-like pain and vomiting. Examination revealed a mass in the right iliac fossa, diagnosed at operation as a carcinoma of the upper jejunum. The tumor was excised with some inches of bowel on either side, and end-to-end jejunostomy was performed. Subsequent microscopic examination gave the true diagnosis. Two and a half years later the patient states that he is in perfect health.

CONCLUSION

The subject of this inquiry was suggested by an observation of W. J. Mayo's (quoted) commenting on the freedom from symptoms enjoyed by several patients, following a first stage short-circuiting operation for ileocæcal tuberculosis. Investigation into the after-history of twelve similar cases similarly treated has shown an identical result, with complete freedom from symptoms, disappearance of the tumor when present, and rapid improvement in general health, in all the cases, at intervals varying from 1 to 4 years after operation.

It is suggested, therefore, in view of these and similar published statistics, that the view generally held, that complete eradication is a *sine qua non* in the effective treatment of this disease is fallacious, and that focal excision, in view of the mortality implicated, is an unnecessary procedure, except in picked, suitable cases.

I am indebted to the honorary surgeons and assistant surgeons of the Manchester Royal Infirmary for permission to investigate their cases, and particularly to Professor E. D. Telford, for his kind help and advice.

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THE EXCRETION OF OVARY STIMULATING HORMONE IN THE URINE DURING PREGNANCY

Its Relation to Urinary Output

DOUGLAS P. MURPHY, M.D., F.A.C.S., Philadelphia
From the Gynecean Hospital Institute of Gynecologic Research, School of Medicine, University of Pennsylvania

THIS report concerns the amount of ovary stimulating hormone which is excreted in the urine during pregnancy, and the effect of alteration in the output of urine upon the rate of excretion of the hormone. No report was found in the literature which recorded the measurement of the hormone in the urine, by the use of the rabbit test of Friedman[1]; and none occurred which dealt with the relation between the output of urine and the excretion of hormone as measured by any method. For these reasons, the present study was undertaken.

EXPERIMENT

The amount of urine passed in 24 hours by a series of 24 pregnant women was measured and the hormone content determined. A correlation between the sizes of the specimens and the amounts of hormone which they contained, forms the basis for the report.

In order to secure accurately collected specimens, passed by normal pregnant women living under uniform physical conditions, an attempt was made to hospitalize an adequate number of such individuals. Failing to secure a sufficient number of normal subjects, it was found necessary to utilize other hospitalized patients, who exhibited mild or moderately severe complications of pregnancy (Table I). All but 2 of the 24 patients were in the middle or last third of gestation (Table III), and all but one were confined to bed on the day that their urine was being collected.

First, a 24 hour specimen was collected from each of the 24 individuals, when on a normal fluid intake; measurement of the hormone in these specimens supplied data on the limits of its excretion. On the following day, 6 of the 24 patients gave a second 24 hour specimen, which was much larger than the first one, due to a forced ingestion of fluids. A comparison of these specimens with the first ones, formed the basis for observations on the influence of urine output on hormone excretion.

Preparation of urine. Each 24 hour specimen of urine was measured, and a sample retained for analysis. A 30 cubic centimeter portion was chilled, acidulated slightly with acetic acid if alkaline, and filtered. It was then well shaken with five volumes of absolute alcohol and the mixture was permitted to stand in the ice box over night. The material was centrifugated, and the supernatant liquid poured off; the residue was air dried and put into normal salt solution, the latter equal in amount to one half of the original volume of chilled urine. This extract was employed as the source for the hormone.

Preparation of animals. Adult female rabbits in the estrous stage, were used for all tests. In order to assure a suitable degree of heat, each animal was permitted to cast a litter, being caged alone from the date of the last successful mating until the end of the experiment. The litter was removed the day of birth, and the animal used for test shortly thereafter.

Hormone unit and method of measurement. The amount of hormone is expressed in rabbit units (Rb.U.). A rabbit unit is defined as that quantity of hormone present in the smallest amount of urine which, on intravenous injection into an estrous rabbit, will be followed by rupture of at least one follicle. In order to discover this amount of urine, a series of rabbits, one animal a day, received graduated intravenous injections of the urine extract until the *maximum non-effective* and *minimum effective* doses were determined. An arbitrary dose was given to the first animal of each series. If follicular rupture was not observed at operation or at necropsy 20 to 24 hours

[1] Friedman, M. H. Mechanism of ovulation in rabbit; ovulation produced by injection of urine from pregnant women. Am. J. Physiol., 1929, xc, 617-622.

TABLE I.—HORMONE EXCRETION AND HEALTH

Recording (1) the amount of ovary stimulating hormone excreted in 24 hours by 24 pregnant women living under similar controlled physical conditions, and (2) the relation of the amount of hormone to the health of the patients. Note the large number of specimens (14 in 24) which contained less than 2,000 rabbit units of hormone, and the fact that the normal patients, and most of the unhealthy ones excreted less than 7,000 rabbit units of hormone.

Thousands of Rb.U.	Urine specimens No.	Health						
		Normal	Mild toxæmia	Threatened abortion	Pyelitis	Diabetes	Cardiac disease	Undetermined
0–1	8	5	1	1	..	..	1	..
1–2	6	..	4	1	1	..	..	..
2–3	2	..	..	..	..	..	1	1
3–4	1	..	..	1	..	..	..	..
4–5	1	..	..	..	1	..	..	..
5–6	2	2	..	..	..	..	..	..
6–7	1	1	..	..	..	..	..	..
7–8	1	..	..	..	..	1	..	..
8–9	0	..	..	..	..	..	..	..
9–10	0	..	..	..	..	..	..	..
10–11	1	..	..	1	..	..	..	..
11–12	0	..	..	..	..	..	..	..
12–13	1	..	..	..	..	1	..	..
Total	24	8	5	4	2	2	2	1

later, the next animal received twice the preceding dose. If the first dose was effective, the following dose was reduced to one-half of the former one. This dosage ratio was employed in all cases, except where amounts of extract exceeding 1 cubic centimeter were necessary. Here the increase of dosage was sometimes less than twice the preceding one. The amount of urine containing 1 rabbit unit is defined as that quantity midway between the maximum and minimum doses described. With this amount of urine determined, the hormone *content* of the 24 hour specimen was computed.

RESULTS

The amount of hormone excreted in 24 hours. The amount of hormone excreted in 24 hours by 24 pregnant women, living under controlled physical conditions and on a normal fluid intake, is recorded in Table I. Though the upper limit of excretion of hormone was in the neighborhood of 14,000 rabbit units, more than 58 per cent of the patients excreted less than 2,000 rabbit units.

TABLE II.—DURATION OF PREGNANCY WHEN URINE WAS MEASURED

Duration of pregnancy, days	Number of patients
0–90	2
91–180	2
181–280	20

TABLE III.—RELATION OF OUTPUT OF URINE TO EXCRETION OF HORMONE

Showing the number of rabbit units of ovary stimulating hormone found in two 24 hour specimens of urine passed by each of 6 pregnant women on succeeding days; the first specimen (A) resulting from a normal intake of fluid, the second one (B) after a forced fluid ingestion. Note the relative constancy of hormone excretion on succeeding days, in spite of wide variation in output of urine.

Patients	Specimen	Urine	Hormone
		c.cm.	Rb.U.
1	A	2500	500
	B	5000	416
2	A	3000	600
	B	6000	375
3	A	2500	278
	B	3600	400
4	A	1250	416
	B	2700	337
5	A	650	1733
	B	2250	1500
6	A	780	195
	B	1400	121

Since most of the patients suffered from complications of pregnancy, and because little is known regarding the relation between them and the excretion of the hormone, their relation is shown in Table I. The normal patients and most of the unhealthy ones excreted less than 7,000 rabbit units.

Three of the pathological conditions are of interest: toxæmia and abortion, because they are peculiar to pregnancy; and diabetes mellitus, because, in the specimens from the diabetic patients an unusually large amount of hormone was present (Table I). Since the amounts of hormone in the first two conditions were not unusual, it appears unlikely that such complicating conditions influence the rate of excretion of the hormone. Whether the presence of diabetes mellitus is related directly to the large amount of hormone, which 2 patients having this disease excreted, requires further investigation.

The relation of output of urine to excretion of hormone. Two 24 hour samples of urine, passed on succeeding days, were collected from 6 individuals. In each instance, the first sample was the smaller, and resulted from a normal intake of fluid; the second larger specimen followed a forced ingestion of fluid. In each case, the 2 specimens varied approximately 100 per cent or more in size (Table III), whereas the amounts of hormone which each contained were about equal. From a comparison of the figures in this table, it appears that the excretion of hormone by the same individual, on succeeding days does not increase with increase in the output of urine, but remains constant. In fact, from a study of these cases, and of 4 which are not recorded, an increase in the output of urine not only was not associated with an increase in the amount of hormone which was excreted, but, if any relation between the two does exist, an increased output of urine was usually associated with a decrease in the excretion of hormone; the latter result, however, is believed to be more apparent than real.

Deductions. The number of observations in this study is small and the patients who supplied urine specimens were not all healthy, nor were they in the same state of pregnancy. Also the number of animals for use was limited. Nevertheless, the results seem to be significant.

It is apparent that the excretion of the hormone is independent of the output of urine; that an increase in the latter has no tendency to wash an additional amount of hormone out of the body. In fact, the reverse may be true. This latter point needs further investigation.

Because the excretion of hormone is constant and the output of urine normally is variable, it follows that the concentration of hormone must vary from sample to sample of urine. Consequently, the excretion of hormone cannot be expressed accurately, if at all, in terms of urine output. It is evident, therefore, that the amount of hormone which is excreted must be measured directly and should represent the amount passed in a suitable period of time in order not to reflect marked alteration upon it by changed physical conditions. For such a measurement, the 24 hour specimen seems most suitable.

The present method of measuring the amount of hormone in the urine is more accurate than other biological ones[2] but like them, possesses too many disadvantages to make it suitable for clinical purposes, though it will continue to have value as a research method. The expense of maintaining a large colony of animals and the time consumed in securing an adequate number of animals in a suitable degree of heat, are two of the chief disadvantages of such a procedure. These combined with death of animals shortly after injection, and the wide variation in the amounts of hormone in the different specimens of urine, which necessitated many unsuccessful measurements before the desired determinations were secured, greatly prolonged the period of the present study.

In spite of these difficulties, additional quantitative estimations of the hormone, either in the urine or blood, or in both, should be carried out, and the normal limits be clearly established, after which the amount in pathological states should be estimated. By such studies light may be thrown on the causes of some of the pathological conditions peculiar to pregnancy, as well as upon the influence of these diseases on production and excretion of hormone.

SUMMARY AND CONCLUSIONS

1. The amount of ovary stimulating hormone (expressed in rabbit units) in 30 24 hour specimens of urine of 24 pregnant women is recorded.

2. Some patients were normal; others exhibited mild complications of pregnancy; the majority were in the last third of gestation when their urine was collected.

3. The amount of hormone excreted in 24 hours varied from less than 100 to more than 12,000 rabbit units; the majority of patients voided less than 2,000 rabbit units.

4. The excretion of hormone by the same individual from day to day was relatively constant and was independent of the output of urine.

5. From these observations, it is concluded that:

[2] Idem. Personal communication.

a. Variation in the output of urine has no significant influence upon the amount of ovary stimulating hormone which is excreted.

b. Estimation of the rate of excretion of ovary stimulating hormone, should be based upon measurement of the hormone in the urine that is passed in a 24 hour period, and not upon the amount in a smaller sample of urine.

The author is greatly indebted to Dr. M. H. Friedman for suggestions and continued assistance throughout the period of investigation.

PROFOUND BLOOD PRESSURE FALL WITH BRADYCARDIA

A NORMAL PULSE RATE IN SURGICAL PROCEDURES[1]

HUBERTA M. LIVINGSTONE, M.D., S. ELIZABETH McFETRIDGE, M.D., AND ROBBIE BRUNNER, M.D.,
CHICAGO

THE pulse is an important factor in determining the general condition of a patient undergoing a surgical procedure. Frequently the person delegated to observe changes in a patient is a nurse, a medical student, or an occasional practitioner whose interest is primarily in the operation. From observation, it appears that the pulse rate as an index of threatened collapse has frequently been overemphasized, and that careful observation is not made of changes in the quality of the pulse. Macleod (1920) speaks of the pulse being rapid during surgical shock. Howell (1927) and Orr (1928) state that the low blood pressure that is characteristic of the condition of shock is associated with a very rapid rate of heart beat. Our data indicates that the pulse is not necessarily rapid during the condition of so called "surgical shock."

Many authors, including Cannon (1923), agree that a state of so called "shock" may be said to exist when the systolic pressure falls to, and remains as low as, 80 millimeters of mercury. Since the use of the sphygmomanometer during surgical procedures has not, as yet, become widely employed, a proper interpretation of the pulse is even more important.

Observations including blood pressure and pulse changes have been made on 268 cases that presented during operation a systolic fall to 80 millimeters of mercury or less. The age incidence was fairly evenly distributed from 1 to 70 years. Three cases were over 70 years of age; 147 cases were male and 121 were female. Novocain, ethylene-oxygen, ethylene-oxygen-ether mixtures, ether, nitrous-oxide gas, cocaine, and spinal anæsthesia were the anæsthetics employed, the last three agents being in the minority. A total of 4,410 operations are included in this series; 2,068 of which were major surgical procedures and 73 were double majors (operations lasting over 3.5 hours). Surgical procedures varied from minor operations as tonsillectomies to major intra-abdominal and brain surgery.

In our series of 268 cases presenting a blood pressure below 80 millimeters mercury, 50 or 18.5 per cent did not exhibit a pulse rate above 100 per minute; 49, or 18.1 per cent, did not have a pulse rate above 120 per minute. In several cases the pulse did not become very compressible, weak, and thready until some time after the blood pressure had reached an alarming level. The greatest age incidence of those not having a pulse rate above 100 per minute, but a low blood pressure, was from 30 to 70 years of age. Of the total cases studied, 57 did not have a blood pressure below 80 millimeters of mercury, but had a rapid pulse rate (above 120 per minute).

In a series of 12 anæsthetized dogs in which death was brought about by hæmorrhage, one dog exhibited no increase in pulse rate, while two had an increase not to exceed 20 per minute (Fig. 1 and Table I). Dogs normally have an increased pulse rate associated with etherization. Following anæsthetization, the 12 dogs observed had a minimum pulse rate of 170.

The early and correct interpretation of collapse during operation, and the resultant early

[1]From the Department of Surgery of The University of Chicago.

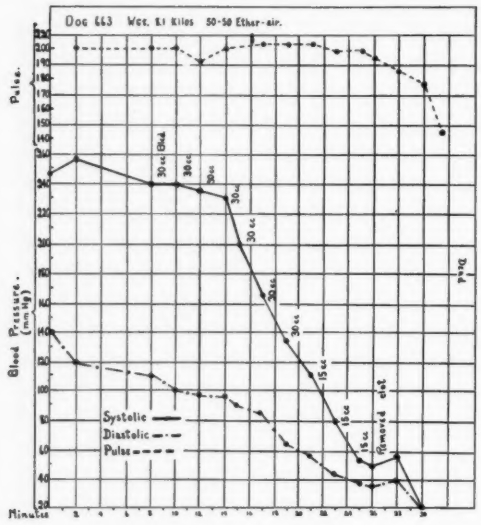

Fig. 1.

administration of stimulants and intravenous normal salt, Ringer's solution, blood transfusion, etc., play an important rôle in the post-operative course. A survey of some of the surgical services during a specific period, including a few case reports, may demonstrate the importance of observing blood pressure and pulse quality changes, rather than changes in pulse rate.

Table II presents the neurosurgical operations. Of the 108 intracranial cases 74 exhibited a systolic blood pressure of 80 or less. Nine or 12 per cent of these did not have a pulse rate above 120 per minute. Of the 83 encephalograms, 9 had a systolic pressure of 80 or less. It is of interest to note that all of these 9 cases did not have a pulse rate above 100 per minute. Sixteen of the 31 spinal cord operations had a marked fall in blood pressure, associated in 7 cases with a slow pulse rate. The following case report illustrates this group:

No. 7395. A woman 70 years of age, entered the hospital on February 2, 1930, complaining that she had had pain across her back and down her legs for 9 months. Physical examination revealed a large, well preserved individual weighing 48.4 kilograms. The blood pressure was 170/105, although the heart sounds were regular in force and rhythm and without murmurs. A roentgenogram revealed a heart 28 per cent oversize with calcification of the abdominal aorta. The lungs were clear, although tuberculous glands were excised from the neck in July, 1929. Blood examination revealed: red blood cells, 4,800,000; hæmoglobin 86 per cent; white blood cells, 9,500. Wassermann and Kahn tests were negative. There was a considerable quantity of albumin in the urine. A pre-operative diagnosis of cord tumor was made.

On March 4, 1930, a laminectomy was performed. Ethylene-oxygen induction was followed by a 4½ ounce ether anæsthesia. Ether vapor was administered intermittently because of a narrow anæsthetic margin and a tendency to cyanosis. There was a thick mucous discharge from the upper respiratory tract which was removed with suction. During the last 40 minutes of the 2 hour operation, the blood pressure was 80 millimeters of mercury or less

TABLE I.—DOG 663. WEIGHT 8.1 KILOGRAMS. NO PREMEDICATION. 50-50 ETHER AIR ANÆSTHESIA. HÆMORRHAGE

Time interval in minutes	Amount bled c.cm.	Blood pressure	Pulse
		246/140 258/120	200
6		240/110	200
2	30	240/100	200
2	30	236/98	192
2	30	228/96	200
1	30	200/90	200
2	30	164/84	208
2	30	132/64	208
2	30	110/58	208
2	15	80/44	200
2	15	56/38	200
1	15	52/36	196
2	Removed clot	58/38	184
2	None		176
1	None		144
2	Dog dead		

TABLE II.—NEUROSURGICAL OPERATIONS

Operation	No.	Systolic BP 80 or less		Pulse 100 or less		Pulse 120 or less		Systolic BP above 80 Rapid pulse	
		Cases	Per cent	Cases	Per cent	Cases	Per cent	Cases	Per cent
Intracranial	108	74	68	3	2.7	6	5.4	10	9.2
Ventricular punctures	53	1							
Encephalogram	83	9	10.8	6	7.2	3	3.6	None	
Retro-gasserian	19	3		1		2		None	
Spinal cord	31	16	51.2	1	3.2	6	19.2	None	

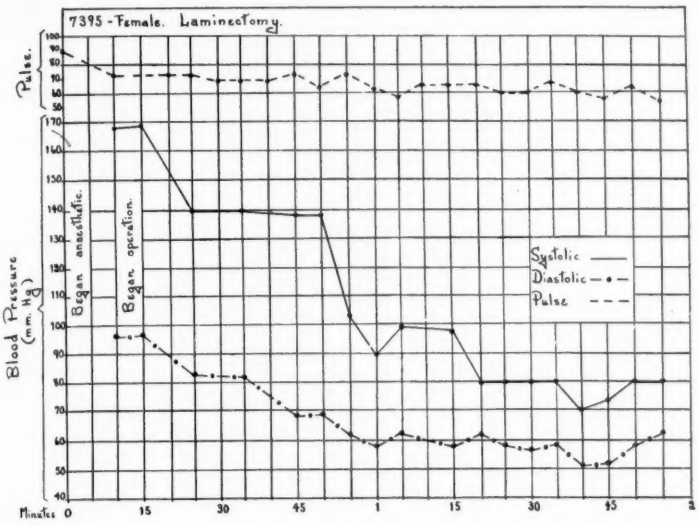

Fig. 2.

systolic (Fig. 2). The pulse throughout remained slow and regular, varying from 52 to 72 per minute. This patient required intensive intravenous therapy immediately after operation to bring the blood pressure and pulse quality back to a normal level. On March 8, 1930, the urine was normal and remained so throughout her stay in the hospital. She was discharged on May 23, 1930.

In 199 major upper abdominal operations, 31 or 15.5 per cent, exhibited a blood pressure below 80 systolic. Of these, 8 or 25.6 per cent did not have a pulse rate above 100 per minute while 12 or 38.4 per cent did not have a pulse rate above 120 per minute. Of the 199 cases, 7 or 3.5 per cent did not have a blood pressure below 80 systolic, but had a rapid pulse (above 120 per minute). The marked blood pressure fall in this group usually occurred when the peritoneum was opened, or during traction or irritation of the upper abdominal viscera, especially in the liver or diaphragmatic area. This effect is in accordance with some phases of the work of Carlson and Luckhardt (1921) in frogs, and Scott and Ivy (1932) in frogs and dogs. Recovery usually occurred with lessening of the traction or trauma, or at least with peritoneal closure. Contrary to the observations of Crile (1903), who reports that the fall in blood pressure with upper abdominal manipulation is associated with a rapid pulse, we found that the pulse rate usually remains low or even falls below normal. The following case report demonstrates this observation:

No. 36686. A housewife, aged 57 years, entered the University of Chicago Clinics on April 10, 1931, because of itching for 8 years, loss of weight for 6 months, diarrhœa for 2 months, pain in the abdomen for 4 weeks, and jaundice for 1 month.

Physical examination revealed a well developed, short, obese woman weighing 85.8 kilograms and 145 centimeters in height. The heart was normal and the blood pressure was 136/72. The lungs presented slight decreased resonance at the right apex. Enlarged tonsils, extensive varicosities of the legs, a femoral hernia, as well as an apparent non-tender mass in the right upper quadrant were present. The sclera were yellow. Blood examination revealed: red blood cells, 5,160,000; hemoglobin 90 per cent; white blood cells, 6,100. Wassermann, Kahn and urine examination were negative. The pre-operative diagnosis was chronic cholecystitis and cholelithiasis.

On June 2, 1931, a cholecystectomy was performed under ether anæsthesia following ethylene-oxygen induction. Eight ounces, open drop, ether was administered. The anæsthetic lasted 2 hours, during the last 1 hour and 35 minutes of which the blood pressure was below 80 systolic, although the pulse rate never exceeded 108 per minute (Fig. 3). The patient received 1 cubic centimeter of ephedrine (hypodermically) during operation and 2 cubic centimeters caffeine sodium benzoate (hypodermically) at the close of operation. She was hyperventilated for a short period with carbon dioxide 10 per cent, oxygen 90 per cent before leaving the operating room.

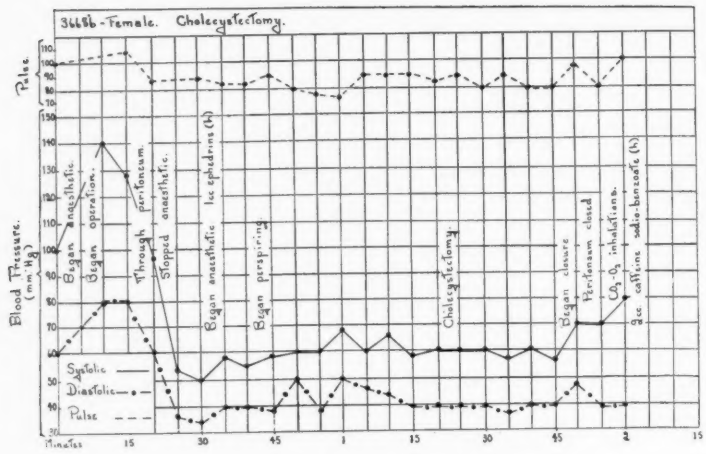

Fig. 3.

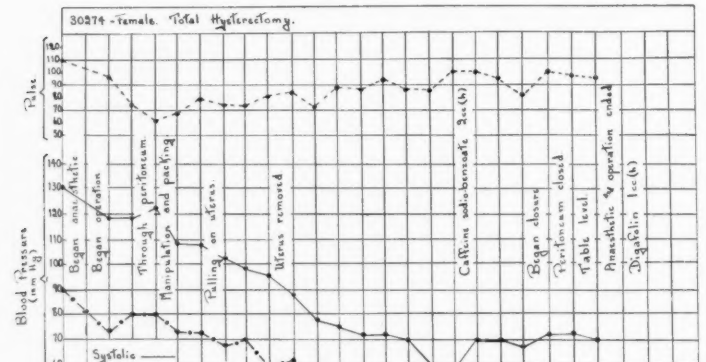

Fig. 4.

The patient was returned to her room in only fair condition. The skin was warm and moist, and the color was fair, but the pulse was very weak, although the rate was 60 per minute. Ringer's solution, 1500 cubic centimeters was administered by hypodermoclysis, the pulse rate increased from 96 to 118 per minute, and the blood pressure rose to 100/60. The pulse also became stronger and of better quality.

Eight hours later 1500 cubic centimeters of Ringer's solution was administered by hypodermoclysis. There was a gradual fall in blood pressure until 5 hours later it was 84/60 and the pulse was 100 per minute and weak in quality. Adrenalin, 1 cubic centimeter, was administered hypodermically and the patient's condition improved. At 1 p.m. the following day the blood pressure was 86/64 and pulse rate 120, so 1500 cubic centimeters of Ringer's solution was again administered by hypodermoclysis. At 4 p.m., although the blood pressure was 98/54, the pulse was weak and thready and the rate had increased to 144 per minute. A 300 cubic centimeter blood transfusion was given. At 6:30 the patient's condition was considered only fair, although the blood pressure was 94/62 and the pulse 116 per minute. One week later the patient was feeling very well, but because of some loss of blood around the cigarette drain and from the center of the wound she was given 500 cubic centimeters blood and 200 cubic centimeters normal salt intravenously. The blood pressure was now 108/65 and the patient made an uneventful recovery.

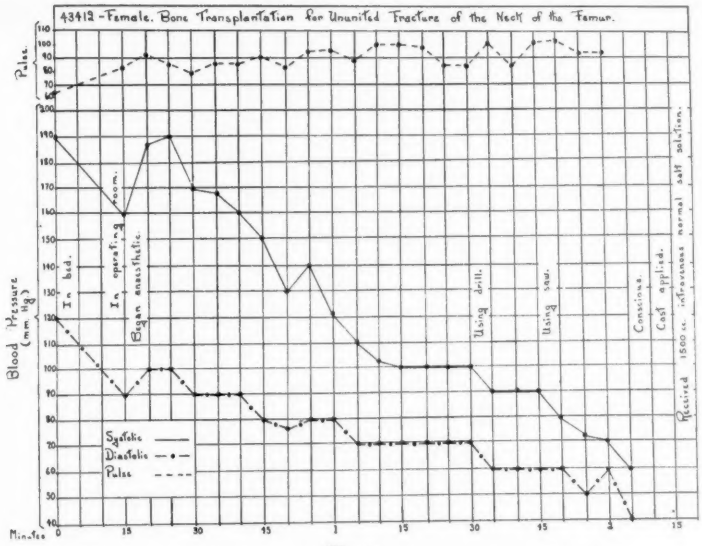

Fig. 5.

On July 16, 1931, patient successfully underwent an operation under local anæsthesia for the repair of the femoral hernia. Except for a pulse that was irregular in quality and rate the operation was uneventful. She was discharged in good condition on July 30, 1931.

De Lee (1928) states that in cases of ruptured ectopic pregnancy, there usually is a low blood pressure and a fast pulse, but he has observed in a few cases a drop in blood pressure associated with a slow pulse rate—in 1 case 46 per minute.

In 213 major gynecological operations, 23 or 10.8 per cent had a low blood pressure. Of these, 8 or 34.7 per cent had a pulse rate below 100 per minute, while the same number had a pulse rate not to exceed 120 per minute. In the following case, the steady fall in blood pressure is associated with a slow pulse rate:

No. 30274. A housekeeper, aged 54 years, came to the University of Chicago Clinics on November 7, 1931, because of continued vaginal discharge and bleeding for 18 months and pain in the legs and back for 1 month.

Physical examination revealed a well developed woman weighing 49 kilograms. The heart was of normal size. The heart rate was slightly accelerated, but regular. The blood pressure was 148/104. The lungs were normal. Blood examination revealed: red blood cells, 4,310,000; hæmoglobin, 75 per cent; white blood cells, 13,350. The urine was normal. The pre-operative diagnosis was suspected carcinoma of the corpus uteri.

On the day following admission, because of a mild febrile reaction, only a dilatation and curettage and examination were performed under a 20 minute ethylene-oxygen anæsthesia.

Four days later (November 12, 1930) the febrile course had subsided, so a total hysterectomy was performed. After a pre-operative 0.010 gram of morphine and 0.0004 gram of hyoscine, ethylene-oxygen with the addition of ½ ounce of ether was administered for 1 hour and 55 minutes. The blood loss was minimal. Following the removal of the uterus there was a noticeable drop in blood pressure, which 35 minutes later was 60/40 (Fig. 4). The pulse rate was 88, regular and of fair quality. The skin was warm and dry. Caffeine sodium benzoate (2 cubic centimeters) was given hypodermically; however, there was but a slight increase in the blood pressure. At the termination of the operation 35 minutes later, the blood pressure was 70/58, the pulse rate 96 per minute and of only fair quality. The patient's body was still warm, but she responded slowly. One cubic centimeter of digifolin was given hypodermically.

Immediately upon returning to her room, the patient was given 1 cubic centimeter digifolin, and 1 cubic centimeter ephedrine hypodermically and 1500 cubic centimeters Ringer's solution by hypodermoclysis. Patient was conscious. Thirty minutes later the blood pressure was 90/70 and the pulse was hardly perceptible. As the pulse remained weak 1 hour later, 500 cubic centimeters of 10 per cent glucose were administered intravenously, and the pulse became stronger. The pulse rate was 94 per minute and the blood pressure 100/70. Eight hours

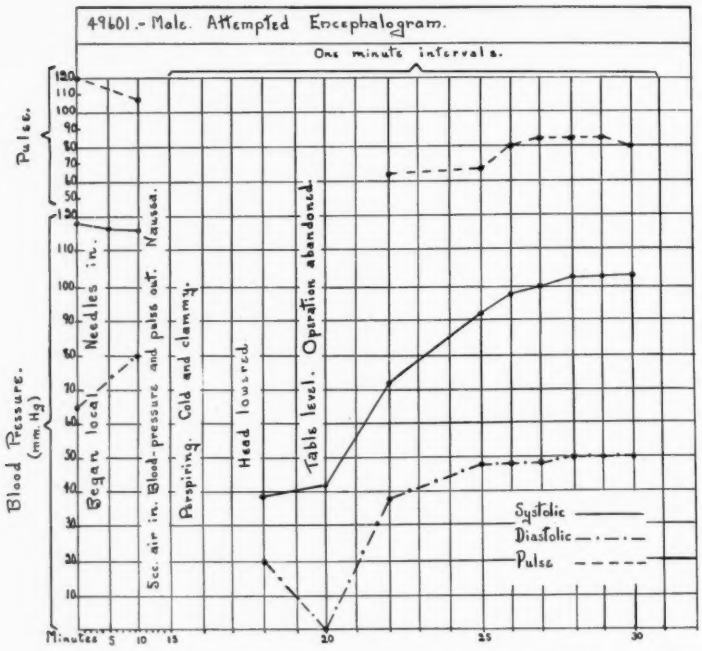

Fig. 6.

later the blood pressure was 124/100; however, the skin was cold and clammy and the pulse almost imperceptible. Codeine and allonal were administered, but the patient did not sleep for 24 hours following operation. The day after operation 1500 cubic centimeters of subcutaneous Ringer's solution were administered as the patient seemed dehydrated. The pulse was now of good quality, and the patient made an uneventful recovery.

In 115 bladder and prostate operations, 8 or 6.9 per cent had a blood pressure below 80 systolic. All of these 8 patients had an associated slow pulse rate, it being below 100 per minute in 6 instances. This group consisted of individuals from 50 to 70 years of age. All presented a moderate to an advanced degree of arteriosclerosis.

Only 3 of 26 kidney operations were associated with a marked fall in blood pressure. Two of these 3 also had a slow pulse.

Table III presents cases not previously discussed and illustrates the frequency with which a low blood pressure was associated with a slow pulse rate.

Wiggers (1923) states that the arterial blood pressure fall in hæmorrhage is associated with a rapid pulse. Although we found hæmorrhage to be frequently associated with a blood pressure fall and pulse rise, we have noted several instances where the blood pressure fall is not associated with a pulse rise. Figure 5 illustrates the reaction to hæmorrhage in a woman 54 years of age undergoing open reduction and fixation with bone transplantation for ununited fracture of the neck of the femur under ethylene-oxygen anæsthesia, preceded by morphine sulphate gram 0.010 and atropine sulphate gram 0.0004. The patient required 1500 cubic centimeters normal salt solution intravenously in the operating room following operation to bring her blood pressure and general condition back to a satisfactory level. Preceding operation, this patient had a blood pressure of 188/120. For the first week following operation the highest blood pressure reading was 120/78. The postoperative pulse was normal.

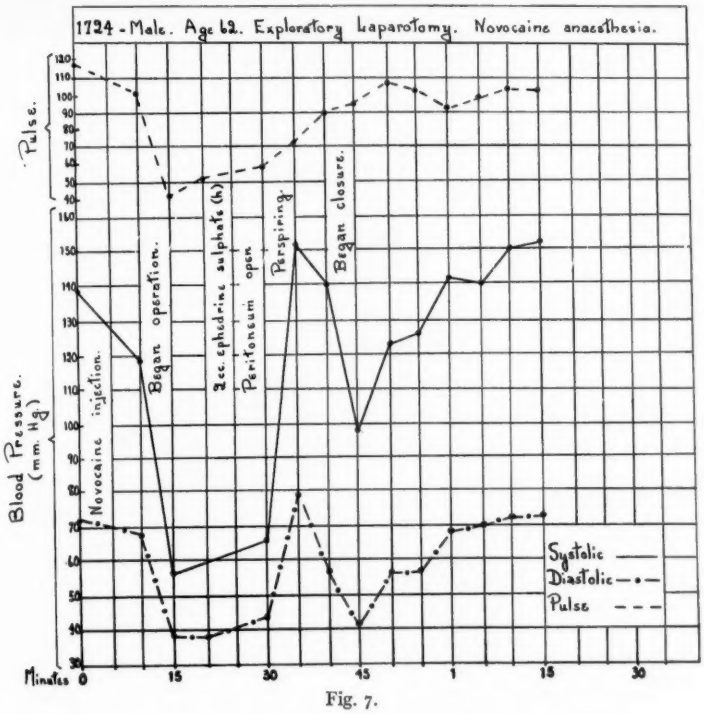

Fig. 7.

Does general anæsthesia remove the changes in blood pressure and pulse rate produced by the fear of the operation or the anæsthesia? Toxic thyroids usually develop a more stable blood pressure and pulse after the induction of general (ethylene-oxygen) anæsthesia. Fear may cause either a rise or a fall in blood pressure with usually an associated rise in pulse rate.

The blood pressure fall that occasionally occurs under local anæsthesia may be attributed to a toxic reaction from the anæsthetic agent employed. According to Eggleston and Hatcher (1919), intravenous administration in cats of toxic doses of cocaine and procaine produces an abrupt fall of blood pressure with a slow heart usually, due to weakening of the heart muscle. They also report one case of intoxication in a woman following novocain injection, with the development of clonic convulsions and slowing of the pulse 8 minutes later. We have never observed convulsive phenomena.

TABLE III

Operations	No.	BP below 80 (Per cent of total)		BP 80 or less pulse 100 or less		BP 80 or less pulse 120 or less		BP above 80 pulse above 120	
Lower Abdomen		Cases	Per cent	Cases	Per cent	Cases	Per cent	Cases	Per cent
Gynecology	214	23	10.8	8	3.7	8	3.7	4	0.9
Bowel resection	5	1		1	20.0	None		4	80.0
Abdominoperineal resection	25	9	36.0	None		None		1	4.0
Miscellaneous	259	3	1.1	2	0.7	1	0.4	1	0.4
Ventral hernia	10	3	30.0	1	10.0	1	10.0	None	
General surgical bone cases	448	68	15.0	7	1.6	6	1.3	20	4.5
Extremity amputation	13	1	7.7	None		None		1	7.7
Breast amputation	36	5	13.8	2	5.5	None		None	
Sarcomata	45	8	17.6	3	6.6	2	4.4	1	2.2
Thyroid	141	5	3.5	2	1.4	None		4	2.8

The possibility of a fainting or psychic reaction has to be excluded. We have observed a

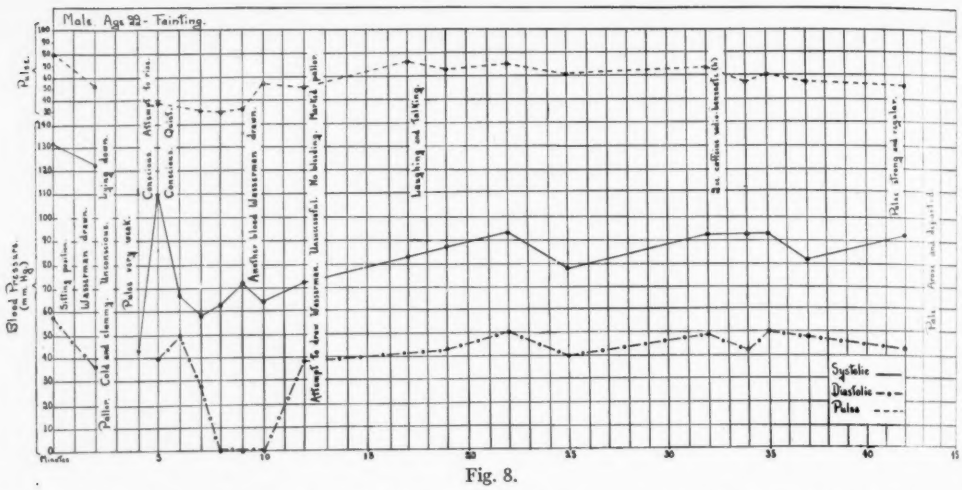

Fig. 8.

slowing in pulse rate associated with a rapid fall in blood pressure both in patients under local anæsthesia, and in very apprehensive or fainting individuals where no anæsthetic agent is employed.

The manifestations mentioned of a slowing in pulse rate associated with a marked drop in blood pressure occurred in patients in both the upright and recumbent positions. Figure 6 illustrates the slowing and weakening of the pulse until it was imperceptible associated with a marked fall in blood pressure 5 minutes after novocain infiltration for an attempted encephalogram. Nausea, pallor, and cold, clammy perspiration were associated with the pulse and blood pressure changes. A comparable picture was seen in a brief study made of tonsillectomies under cocaine anæsthesia. The sitting position was employed in these two types of surgery. The same reactions have been observed in patients in the recumbent position under novocain anæsthesia (Fig. 7).

In order to eliminate the possibility of a toxic reaction from the anæsthetic agent employed, studies of the blood pressure and pulse changes during the drawing of blood for Wassermann and Kahn tests were made. Of 44 cases studied, 5 had a marked drop in blood pressure and a slowing of the pulse rate, and one patient lost consciousness. The rapid blood pressure fall that occurs with syncope has been reported (Tocantins, 1930). Figure 8 illustrates not only the loss of blood pressure sounds with a loss of consciousness in fainting, but also the slowing to loss of pulse beat. Upon the return to consciousness there was a rapid return of blood pressure and a slow increase in pulse rate. Forty minutes later neither pulse nor blood pressure had reached a normal level.

A blood pressure fall was observed in a patient 18 years of age during the excision of a sinus of the buttocks. No anæsthetic agent was employed because of the presence of sacral anæsthesia resulting from a spina bifida.

It is of interest to note the changes in pulse and blood pressure associated with the use of a constrictor. The application of the constrictor usually does not produce much change in blood pressure. There may be some rise, especially if the patient is not entirely anæsthetized. Operation on the bloodless area, as for osteomyelitis in adults, usually does not cause a blood pressure fall. In children, a very gradual fall may occur. After removal of the constrictor, in a small number there is no change in blood pressure and pulse. Of 75 cases 65 had a fall in blood pressure. Of these 31 had a fall in pulse rate; 27 had no change in pulse rate; while 10 had a pulse rise.

DEDUCTIONS

Frequent instances have been presented where the drop in blood pressure has been our earliest warning of a change in the patient's

general condition. This suggests the importance of the more frequent employment of blood pressure observations during surgical procedures, to enable us to institute earlier restorative measures. The time factor is of great importance as regards improvement in the patient's general condition, when the need arises for stimulants, intravenous fluids, and blood transfusion. The rapid improvement following the timely administration of a blood transfusion is noteworthy. It is apparent that changes in the quality of the pulse must be carefully observed, as well as changes in the pulse rate.

SUMMARY

A marked blood pressure fall may occur without an increase in pulse rate.

A patient's condition may reach an alarming level some time before an increase in pulse rate occurs.

Blood pressure changes, rather than an increase in pulse rate, frequently present the earliest evidence of circulatory failure.

NOTE.—This work was done under the direction of Professors D. B. Phemister and Edmund Andrews, whom the writer wishes to thank for their many helpful suggestions.

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CLINICAL SURGERY

FROM THE I SURGICAL CLINIC, BUDAPEST, T. VEREBELY, DIRECTOR

RESECTION OF THE STOMACH

END-RESULTS IN 2,400 CASES

EDWARD C. EMERSON, M.D., SAINT PAUL, MINNESOTA
AND
LADISLAUS CZIRER, M.D., BUDAPEST, HUNGARY

IN the treatment of gastric and duodenal lesions resection of the stomach has been, for many years, the most important surgical procedure used in the majority of European surgical clinics. A variety of methods have been employed, the majority being modifications of the Billroth I and II resections.

This paper presents a statistical summary of 2,400 consecutive resections performed in this clinic up to May 1, 1932. To remove ulcers 1,500 resections were performed and 900 resections were done for malignancy. Practically all the ulcer patients had received careful medical treatment before they were referred to this clinic for surgery.

Resection of the stomach is indicated in the presence of (1) stenosis, (2) perforation of the ulcer, (3) recurrent profuse bleeding, and (4) removal of a calloused ulcer remaining after dietary treatment.

Of the ulcer patients operated upon, the ulcer incidence is over three times greater in the male than in the female—78.7 per cent males, 21.3 per cent females. The most common site of the lesion was the pylorus and duodenum; 34.9 per cent for the latter and 32.3 per cent for the former. In 15.9 per cent of the cases the lesions were on the lesser curvature; in 12.3 per cent there was an associated stenosis; and in 4.1 per cent there were multiple lesions.

As to the age incidence patients between 30 to 40 years were the most commonly affected, making 29.9 per cent of the total; 27.3 per cent were between 40 to 50; 17.9 per cent between 20 to 30; 17.2 per cent between 50 to 60; 6.3 per cent over 60, and the smallest percentage, 1.4 per cent, were between 10 to 20 (Fig. 1).

The operative treatment which is used in this clinic is essentially that developed by Billroth. Ulcer is considered to be more than a localized lesion and therefore requires more than local excision or palliative gastro-enterostomy. All calloused ulcers of the stomach are resected.

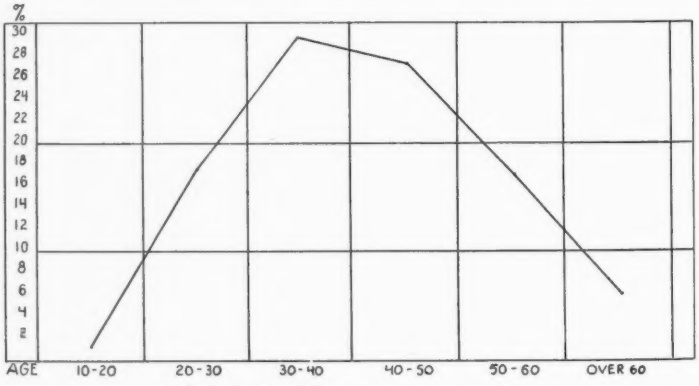

Fig. 1. Age incidence in 1,500 resected ulcers.

Fig. 2. Gastric erosion.

Sections of resected stomachs taken beyond the ulcer proper show in most cases evidence of gastritis with hyperacidity, gastric erosion, and a marked increase in number and size of follicles (Fig. 2). Therefore, because of this abnormal change in the gastric mucosa, resection is considered the best form of treatment.

In many cases of early gastric cancer diagnosis as such cannot be made until after operation. Pommershiem, of this clinic, found 47 cases of carcinoma superimposed on old calloused ulcers in a total of 530 patients examined, or about 9 per cent.

TABLE I.—POMMERSHIEM'S STATISTICS

	Per cent
Ulcer associated with gastritis	
Hypertrophic	46
Atrophic	40
Mixed	3
Site of ulcer	
Lesser curvature	46
Prepyloric	28
Pyloric	26
Depth of ulcer	
Submucous	5
Calloused	72
Penetrating	23
Microscopic appearance of ulcer	
Carcinoma solidum	40
Adenomatous	57
Fibrosum	3
Type of ulcer	
Single	92.5
Duplicate	2.5
Triplicate	5

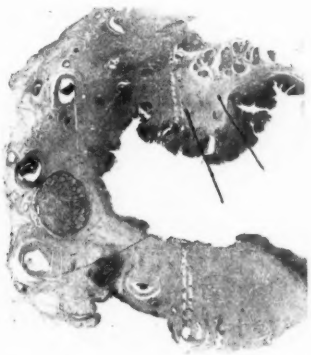

Fig. 3. Papillary degeneration, old calloused ulcer. Precancerous lesion.

Clairmont states that about 10 per cent of calloused gastric ulcers become malignant, but that 50 per cent of those which are prepyloric have a predisposition to malignancy. A. J. Walton believes that 10 per cent of gastric ulcers become malignant; Maresch considers the incidence to be between 10 to 15 per cent. Accepting as a fact that a certain percentage of gastric ulcers become malignant, resection offers the best chance of cure (Figs. 3 to 8).

Figure 3 shows a gross section of an old calloused ulcer at the precancerous stage. There is a decided papillary overgrowth and Figure 4 (microscopic section) shows the earliest change which we can regard as beginning cancer. A further advanced lesion is seen in Figure 5, also with history of a long standing ulcer on the lesser

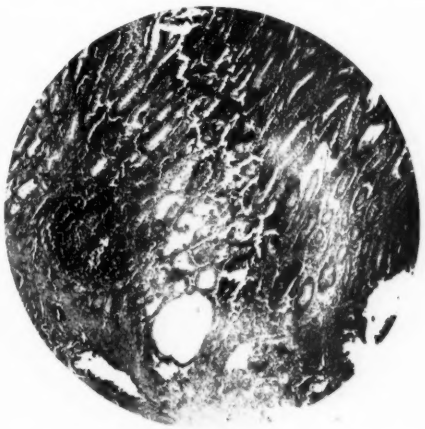

Fig. 4. Microscopic appearance of preceding ulcer.

Fig. 5. Carcinoma of lesser curvature.

curvature. Figure 6 shows the gross, and Figure 7, the microscopic appearance of the ulcer with definite carcinomatous change. Both of these cases were diagnosed by X-ray examination as

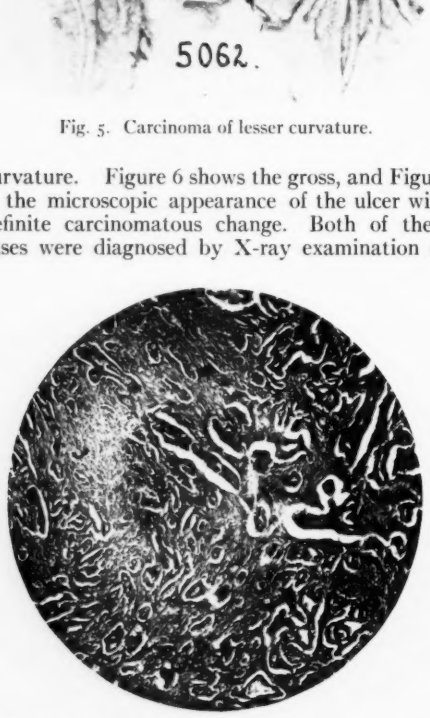

Fig. 7. Carcinomatous ulcer. Microscopic appearance of preceding ulcer.

Fig. 6. Carcinomatous ulcer. X-ray diagnosis of ulcer of lesser curvature 6 years before operation, medical treatment in interval.

ulcer of the lesser curvature 5 and 6 years previous to operation. A further similarity between the papillary degeneration of an old ulcer and cancer is demonstrated in Figures 8 and 9.

The detailed technique of Professor Verebely's method of stomach resection was first reported in 1927 by Neuber. He reported results on 226 cases operated upon up to that time. To review briefly without a detailed report as to pre-operative care, anæsthesia, and step by step procedure, I will mention only the general principles which are embodied in this method:

1. Application of the sewing clamp to the stomach after ligature of the vessels (Figs. 10A and 10B).

2. Incision between two rows of metal sutures preventing escape of any gastric content (Fig. 11).

3. Removal of stomach and portion of duodenum (containing ulcer when possible[1]).

4. Closure of duodenum—continuous catgut for the muscularis and mucosa, and interrupted sutures for the serosa.

5. Anastomosis between stomach and jejunum, the lower corner of stomach is resected, suture *line fixed below* and through mesocolon (Fig. 12).

The operation is performed under local anæsthesia—usually splanchnic anæsthesia is employed though spinal and infiltration methods have also been used.

After this method of resection, all patients are sent to the X-ray laboratory for fluoroscopic examination on the eighth or tenth postoperative day. Dr. Ratkoczy, director, has found that there is no precipitate emptying of the stomach.

[1] When it is not possible to excise duodenum below ulcer the method of Finsterer is followed, resection by exclusion of the ulcer.

Fig. 8. Papillary degeneration of gastric mucosa.

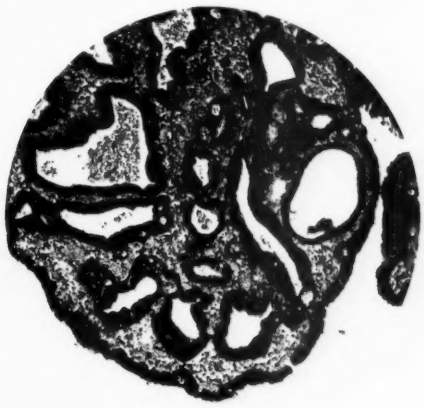

Fig. 9. Papillary carcinoma.

The metal sutures have in no case caused any difficulty; they usually slough out and are passed by bowel in 2 or 3 weeks.

The mortality for all cases following gastric resection was 7.8 per cent; following gastro-enterostomy 3.5 per cent. Since 1923, the corner anastomosis of Professor Verebely has been exclusively followed, and the mortality has been lowered to 4.8 per cent. This is inclusive for all resections, for carcinoma, perforated ulcers, etc. In operation for peptic ulcer alone, the mortality was 4.5 per cent following gastro-enterostomy; 18 per cent after exclusion of pylorus and gastro-enterostomy; and now 0.5 per cent after resection with the use of the sewing clamp and corner anastomosis.

Any method of treatment can be fairly judged not alone on the mortality statistics but by the end-results obtained especially if the method has been used in a large number of cases over a long period of time and the follow up shows continued good results. Since 1923, a careful postoperative check-up has been made on all patients on whom resections were performed. Previous to that time, postoperative records on ulcer and cancer patients operated upon had been kept, but the data were not as complete. The sum total of all resections performed has shown good results in 81.4 per cent of the cases, or 1,954; fair results 16.6 per cent, or 398 cases; bad results 2 per cent, or 48 cases.

After palliative operations—exclusion with gastro-enterostomy, etc.—we found good results in 49 per cent, fair results in 33 per cent, and bad results in 18 per cent.

After resection with corner anastomosis accord-

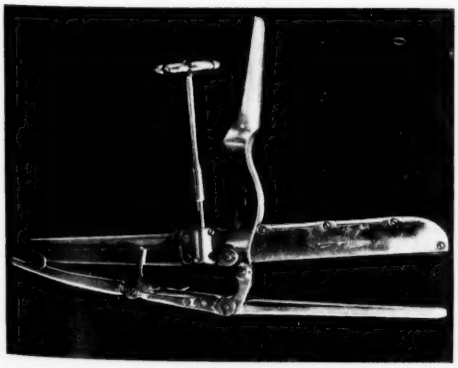

Fig. 10. A, Sewing clamp to be applied to stomach. B, Application of sewing clamp to stomach (from movie film).

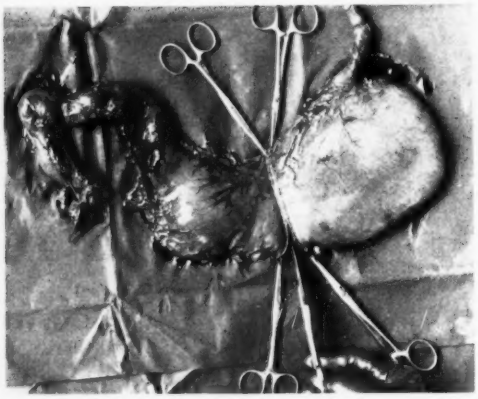

Fig. 11. Stomach incised between two rows of metal sutures.

Fig. 12. Corner of stomach to be resected followed by anastomosis to jejunum.

ing to Professor Verebely, good results were obtained in 90 per cent, fair results in 8.5 per cent, poor results in 1.5 per cent.

CONCLUSION

A method of treatment is reviewed and the results after a 9 year period have been summarized and have been found to be more satisfactory both in regard to mortality and permanency than are the results from any of the other methods of treatment.

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OVARIAN TUMORS OF THYROID TISSUE

JAMES C. MASSON, M.D., F.A.C.S., ROCHESTER, MINNESOTA
Division of Surgery, The Mayo Clinic

SELMA C. MUELLER, M.D., ROCHESTER, MINNESOTA
Fellow in Medicine, The Mayo Foundation

ACCESSORY thyroid glands or aberrant nodules of thyroid tissue are found comparatively frequently in the neck, base of the tongue, and structures of the thorax. Also cell masses identifiable as thyroid tissue are not infrequently noted in ovarian dermoid cysts or teratomata (19 per cent according to Koucky). But isolated nodules of thyroid tissue in the ovary unassociated with other heterotopic tissues are so rarely seen that their occurrence deserves to be recorded.

The significance of thyroid tissue in the ovary, in which thyroid structures make up practically all of the tumor, has been widely considered. Gottschalk, in 1899, described a tumor of the ovary, which he believed had arisen from malignant change in a graafian follicle. His description corresponded to that of a tumor of thyroid tissue, but he called it "folliculoma malignum ovarii." Kretschmar, in 1901, reported a similar tumor in which he believed he could demonstrate the primary tumor elements arising from the lining cells of a lymph space. He, therefore, designated the tumor an endothelioma. Katsurada, also in 1901, described briefly a teratoma containing thyroid tissue. The following year Pick presented before the Berliner medizinische Gesellschaft a series of 21 dermoid tumors of the ovary, 7 of which contained thyroid tissue. His evidence was convincing that the thyroid tissue in these tumors was part of a teratomatous growth in which the endodermal elements of thyroid anlage had undergone excessive development with partial or complete suppression of other tissue elements. He placed the cases of Gottschalk and Kretschmar in the same category. This gave rise to a series of heated arguments before this society. Kretschmar later admitted that his tumor consisted of thyroid tissue, but he believed that it had metastasized, in spite of the fact that a few small areas of bony tissue were found. He explained these on the basis of metaplasia of the connective tissue. Following Pick's intensive study of this type of tumor and of teratomata in general, numerous studies were reported from various countries. Most observers supported the teratomatous origin of these tumors. Walthard made serial sections of three ovarian tumors which grossly seemed to consist only of thyroid tissue. In one of these he found a small, cartilaginous mass, and in another a small area of squamous epithelium and sebaceous and sweat glands. The third and largest tumor consisted of thyroid tissue except for a little ovarian stroma in the capsule. This work gave material support to Pick's hypothesis. Saxer, about the same time, contributed additional evidence by describing his frequently quoted case, the ovary of which was entirely normal except for the inclusion of a single tooth; thus a dental anlage had developed with suppression of all other types of tissue.

Bauer and Borst, among others, have refuted the teratomatous origin of these tumors. Bauer demonstrated a transition from a typical papillary cystadenoma into thyroid-like tissue, and stated his belief that most so called tumors of thyroid tissue of the ovary are atypical cystadenomata. Borst presented the view that a follicular adenoma might give rise to thyroid characteristics, and have nothing to do with a teratoma. In this regard, the view of Ribbert may be recalled that cystadenomata of the ovary are teratomatous in origin, having an endodermal anlage, and are therefore frequently associated with dermoid cysts. Bell did not accept this view, since he believes that the thyroid-like tumors arise from a peculiar colloid degeneration of cystadenomata. Strong is inclined to agree with this view, except in rare instances. However, most observers agree with Pick that these tumors are of teratomatous origin.

To the clinician, the most interesting feature of this type of tumor is its capacity for secreting thyroxin. Certainly in most of the cases reported the presence of hyperthyroidism was not mentioned. Frankl explained this lack of physiological function on the basis of a relatively meager interacinar blood supply. The presumable thyroid secretion is thus not adequately absorbed into the blood stream. A few cases have been reported, however, in which some physiological effect was believed to have been demonstrated. Kovács reported the case of a woman, aged 33 years, who had an enlarged thyroid gland and mild symptoms of hyperthyroidism. A tumor of thyroid tissue was removed from the ovary. Nine months

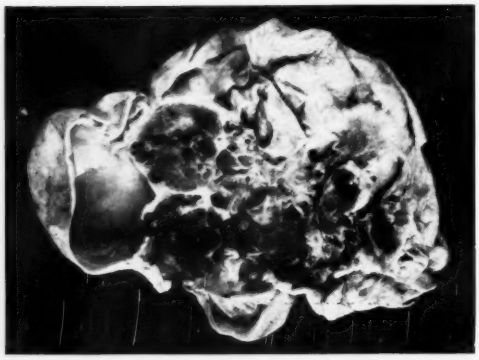

Fig. 1. Ovarian tumor removed at operation. Some of the large peripheral cysts have collapsed but the colloid of the central portions is preserved. The mass measured 14 by 8 by 7 centimeters, and weighed 210 grams. Case 1.

after operation the symptoms of hyperthyroidism had improved. Trapl reported a case in which hyperthyroidism developed after removal of a thyroid tumor from the ovary. He explained this phenomenon as compensatory hyperfunction of the thyroid gland. In a case reported by Moench, a cardiac irregularity which had been considered functional, cleared up after removal of a cyst from the right ovary which was found to contain thyroid tissue. Morgan presented a necropsy report in which a markedly atrophic thyroid gland was associated with a tumor of the left ovary. He believed that the teratomatous thyroid tissue was compensating for the atrophic thyroid gland. Outerbridge, after reviewing all the reported cases, came to the conclusion that the aberrant thyroid tissue has little if any functional significance. It is with this question of functional activity in mind, that the following cases are presented.

REPORT OF CASES

Case 1. A woman, aged 49 years, first came to the clinic September 13, 1929. At this time she gave a history of mild hyperthyroidism. Her highest basal metabolic rate was +15, and the pulse rate was consistently around 100 beats each minute. A pelvic tumor was also noted. She was advised to have thyroidectomy first, and later to have the tumor in the pelvis removed.

September 30, subtotal thyroidectomy was performed with double resection and removal of the isthmus. The pathologist reported hæmorrhagic cystic degenerating colloid and fetal adenoma in a colloid thyroid gland. The tissue removed weighed 36 grams. Recovery was uneventful. October 16, left oophorectomy was performed for multilocular cystic tumor of the left ovary. The pathologist reported that the tumor (Figs. 1 and 2) consisted of hæmorrhagic, fibrous, hyaline, cystic, degenerating colloid and fetal thyroid adenoma. At the time of the operation a great deal of milky ascitic fluid escaped from the abdomen. The patient was dismissed in fair condition 19 days after the operation. The final basal metabolic rate after the two operations was —4.

The patient returned December 11, with marked anasarca which had gradually developed since she left the clinic in October. The only abnormality noted on examinations of the blood and urine was albumin, grade 1, in the urine. Paracentesis was done with removal of 1,700 cubic centimeters of straw colored fluid. The œdema was treated with salyrgan with good response.

Between December 11, 1929, and October 2, 1931, the patient returned to the clinic a number of times for paracentesis and study, always with the same results, except that a renal stone and hæmaturia was discovered on one occasion. Roentgen rays were applied over the pelvis and abdomen without relief of ascites. The patient's general condition remained good in spite of the fact that she had had paracentesis with removal of about 9,500 cubic centimeters of fluid every 10 days.

October 6, 1931, abdominal exploration was carried out. A large amount of ascitic fluid was evacuated, but no other abnormalities were noted. All peritoneal surfaces appeared normal. October 30, after dismissal from hospital, the patient began to complain of severe abdominal cramping, requiring morphine. Ascites and cardiac embarrassment were noted. Her condition gradually became worse and the leucocyte count was high. Death occurred November 1.

Necropsy disclosed a remarkable state, apparently in no way related to the previous hyperthyroidism and ovarian tumor. In addition to 10,000 cubic centimeters of ascitic fluid, there was complete thrombosis of the portal system. The thrombus was recent in the mesenteric veins, but old and well organized and partially canalized in the splenic vein. The left branch of the portal vein at the hilum of the liver was reduced to a fibrous band. The ascites was apparently dependent on the thrombotic process which had suddenly increased, and ended fatally. No recurrence of tumor was noted in the pelvis, all peritoneal surfaces being smooth. Figure 3 shows the structure of the thyroid gland removed at necropsy.

On further study of the cystic ovarian tumor which was removed, ovarian stroma was found only in its peripheral portions; this was infiltrated with lymphocytes. Most of the blocks, cut from various parts of the tumor, contained areas structurally typical of adult thyroid tissue whereas (Fig. 2), in other areas were the small, closely packed acini seen in so called fetal adenoma. Here and there were areas of œdematous and degenerating hyaline stroma containing scattered small groups of thyroid-like acini. Teratomatous structures other than thyroid tissue were not found, except one small cystic space which was lined by an atypical stratified epithelium six to eight cells deep, which may possibly have represented ectodermal elements.

The important question, which unfortunately can never be answered definitely, is whether the patient's hyperthyroidism may not have been partially or completely due to the large mass of thyroid tissue in the left ovary. The weight of the mass, on removal, was 210 grams whereas the tissue removed from the thyroid gland weighed

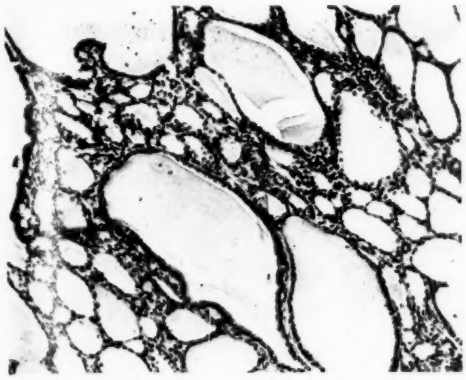

Fig. 2. Ovarian mass in which may be seen evidence of hyperplasia of the thyroid epithelium in some of the larger acini. Case 1.

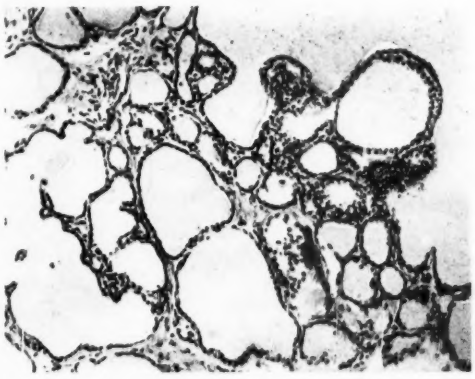

Fig. 3. Specimen of thyroid gland removed at necropsy (Fig. 2). Slight evidence of hyperplasia may be noted. Case 1.

only 36 grams. In the ovarian tumor, occasional areas of hyperplasia were noted (Fig. 2). These were also present in the thyroid gland. It is unfortunate that basal metabolic rates were not taken in the interval between the two operations. The pulse curve after the two operations, however, affords some information. Seven days after the thyroidectomy (first operation) the pulse came down to 90 beats each minute. This was the lowest pulse rate recorded during that period in hospital. The patient was dismissed from the hospital on the eighth day with a pulse rate of 100. Following the removal of the thyroid tumor of the ovary, the pulse rate was 70 on the fifth and sixth postoperative days, and although it did not remain at this level, it maintained a lower level than previously. The basal metabolic rate after both operations was −4, but this is of no assistance in answering the question. The subsequent events, with the rapid reaccumulation of ascites over a period of 2 years, were probably in no way related to the hyperthyroidism, but were no doubt due to portal thrombosis. The basal metabolic rate reported 10 days before death, was −4.

Case 2. A woman, aged 55 years, presented herself at the clinic November 4, 1927, with a history of swelling of the abdomen for 4 months which began following an attack of severe pain in the region of the urinary bladder. The abdomen had been tapped three times before admission with removal of about 9,500 to 11,000 cubic centimeters of fluid each time. She had lost more than 15 pounds in weight during her illness and felt weak, and her appetite was poor. She had passed through a normal menopause at the age of 45 years. There had been no pelvic symptoms until the onset of the present illness when suprapubic pain developed.

On examination, evidence of loss of weight was most apparent about the face, neck, and arms. The thyroid gland was normal to palpation. The heart was normal except for a rapid rate which varied between 80 and 110 before operation. The abdomen was markedly distended with fluid so that organs could not be felt. Pelvic examination likewise was negative. Roentgenograms of the abdomen and thorax, study of chemical changes in the blood as well as tests of hepatic function, all proved to be within normal limits. Achlorhydria was the only abnormal laboratory finding. The basal metabolic rate was not taken. Diuretic response to salyrgan and ammonium nitrate was very slow.

Abdominal exploration was performed November 16 with the withdrawal of a large amount of clear fluid. The liver was normal to palpation, as was the peritoneum. There was a tumor of the right ovary which was somewhat adherent, with considerable inflammatory reaction in the cul-de-sac, but without evidences of malignancy. The tumor was removed, without disturbing the uterus and left ovary. Pathological examination revealed the right ovary to be replaced by a cystic mass weighing 45 grams. It contained a fibroma and tissue which grossly and microscopically resembled adult and fetal thyroid tissue with areas of undifferentiated fetal thyroid tissue (Fig. 4). Certain alveoli showed papillary projections covered with cuboidal or columnar epithelium and typical hyperplasia. In only one area was there any tissue suggestive of ovarian stroma, and this was without follicles.

The patient recovered rather slowly but steadily, and there was no tendency to reaccumulation of fluid. The tendency toward tachycardia continued, although the pulse rate seldom was more than 100 after operation. Compound solution of iodine 30 minims was given for 4 days after operation, and again before the patient left the hospital. Two basal metabolic rates, taken on the thirteenth and twentieth days after operation were +32 and +30, respectively. However, neither of these determinations was considered satisfactory by the technicians. The patient manifested few symptoms of hyperthyroidism, although she was nervous and "jumpy" and the pulse rate was usually above normal. The weight, after operation, with the loss of fluid, was 58 pounds less than the normal weight of 193 pounds. The patient was dismissed feeling well 23 days after operation. She was heard from numerous times until June, 1930, which was 2½ years after operation, and each of these times she reported that her condition was excellent.

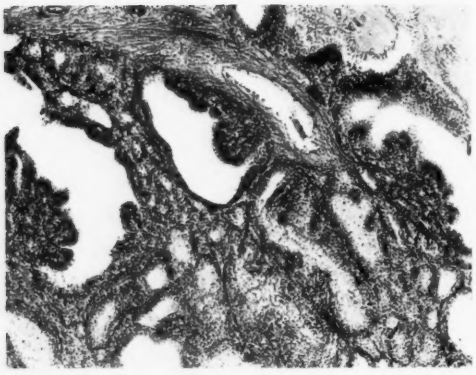

Fig. 4. Frozen section from ovarian tumor. Although this is a thick section, the epithelium may be seen in folds typical of hyperplasia, in the larger acini. Case 2.

Although we have no absolute evidence of hyperthyroidism in this case, we made several suggestive observations, most important of which are tachycardia, marked nervousness, and loss of weight. It is unfortunate that the basal metabolic rate was not taken before operation. Although the two rates taken after operation were not entirely satisfactory, it is probable that the rate was somewhat elevated at that time. The rapid accumulation of ascitic fluid was an interesting feature in this case. Although ascites occurs commonly with malignant ovarian tumors, its occurrence with benign tumors of the ovary is not common. It is said to occur in 7 to 8 per cent of ovarian cystomata, however, and it is possible that the peritoneal irritation produced by the tumors causes the outpouring of fluid. This is a possible explanation in this case, since there was considerable inflammatory reaction in the pelvis about the tumor.

Case 3. A woman, aged 63 years, came to the clinic October 28, 1916, because of constipation. She had always been nervous, and had had a rapid heart beat with slight tremor which had not been progressive.

Examination revealed a pulse rate of 114 beats each minute; the blood pressure in millimeters of mercury was 160 systolic and 60 diastolic. The heart was enlarged slightly to the left. A coarse tremor of the hands was present, which could be partially controlled voluntarily. In the pelvis a firm nodular mass was felt to the right and posterior to the fundus of the uterus.

Subtotal abdominal hysterectomy was performed, with removal of both ovaries and fallopian tubes. The pathologist found that the right ovary had been replaced by a mass of vascular tissue 7 by 6 by 5 centimeters. The cut surface was honeycombed with multiple tiny cysts filled with a colloid substance, and some very firm central masses. On microscopic examination, the mass resembled thyroid tissue both of the fetal and adult types with slight evidences of hyperplasia. The firm central masses were made up of degenerated material containing coarsely granular calcium masses. Ovarian tissue was not identified.

It is unfortunate that metabolic studies were not made in this case, but with some evidences of hyperplasia of the thyroid tissue in the tumor, it is possible that mild hyperthyroidism was present, as evidenced by the tachycardia. The nervousness may have been significant; the tremor of the hands which was partially voluntarily controlled, may also have been partly on a hyperthyroid basis. We have no data on the subsequent course of the case.

Case 4. A woman, aged 39 years, first came to the clinic December 20, 1920, at which time a diagnosis was made of tuberculosis of the third and fourth lumbar vertebræ, adenomatous thyroid gland, without evidences of hyperthyroidism, and a left ovarian tumor which apparently was not causing symptoms after treatment of the spinal column. She was advised to return in 3 months but she did not return until November 8, 1926, when she gave a history of metrorrhagia for 5 months. The adenoma of the thyroid gland was still present, but without apparent symptoms of hyperthyroidism. The tuberculous lesion of the lumbar vertebræ was well healed. The cervix uteri was markedly eroded and cystic, the fundus was somewhat enlarged, and the mass in the left ovary was estimated to be of about the same size as on the previous examination. Dilatation and curettage of the uterus revealed hypertrophic endometritis. The cervix was cauterized. On examination of the pelvis under anæsthesia, further operation was not deemed advisable.

September 28, 1931, the patient returned to the clinic with a history of bloating of the abdomen which had been constant for the last 2 to 3 months. She had gradually gained weight, from 185 to 202 pounds, and noticed a dragging sensation in the pelvis. Examination revealed well marked ascites in addition to obesity and a tumor in left side of the pelvis. A multilocular cyst of the left ovary was removed and a large quantity of ascitic fluid was drained from the peritoneal cavity. The left ovary was found to be replaced by a large multilocular cyst which measured 12 by 9 by 8 centimeters. The largest cyst contained hæmorrhagic material adherent to its wall. The other cysts were smaller, and minute honeycombed cysts made up a large part of the mass. Sections taken from numerous areas of the mass showed groups of variously sized alveoli lined with flat or cuboidal epithelial cells, typical of thyroid tissue (Fig. 5). Masses of small cysts made up the walls of the larger cysts. All were filled with rather deeply staining colloid. Many areas gave the appearance of fetal thyroid tissue whereas others appear definitely hyperplastic. A fairly large irregular mass of polygonal cells with deeply stained nuclei surrounded and penetrated by blood filled spaces, was present in one section (Fig. 6). Here and there was a suggestion of alveolar arrangement. These cells were suggestive of primitive thyroid structure, but this possibility cannot be proved.

Although this patient had an adenomatous goiter, and a large amount of thyroid tissue in the ovary, many areas of which showed evidences of hyperplasia, clinical evidence of hyperthyroidism was not displayed. For this reason, metabolic rates were not determined. One may speculate

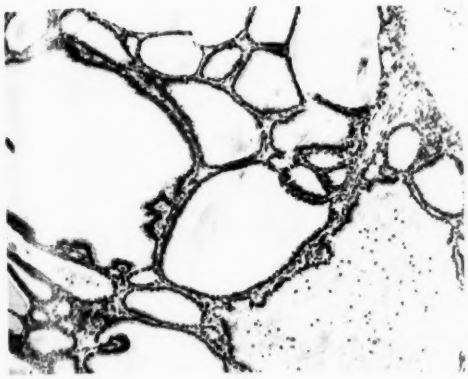

Fig. 5. Typical thyroid structure in ovarian tumor. Hyperplasia is clearly shown in the papillary projections of columnar epithelium into the acinar spaces. Case 4.

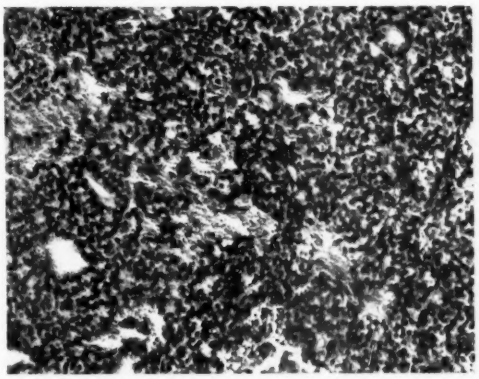

Fig. 6. Mass of polygonal cells resembling parathyroid tissue. The grayish spaces are filled with erythrocytes. Case 4.

concerning the occurrence of cells similar to parathyroid cells, but there is no means of proving the identity of this mass of tissue. We have found reference to a similar type of tumor in the literature. Moench found masses of cells which closely resembled parathyroid cells in a tumor of thyroid tissue of the ovary. This case is included because of the nature of the tumor and the ascites without clinical hyperthyroidism, in spite of definite hyperplasia of the thyroid epithelium in some areas.

CASE 5. A woman, aged 38 years, first came to the clinic February 9, 1931. She had begun to have "heart trouble" in the autumn of 1930. In December she noted a swelling of the neck which increased rapidly. Later her voice changed and she had difficulty in talking. Dyspnœa and occasionally stridor, dysphagia, weakness, nervousness, and loss of weight were among her complaints.

The patient appeared to be mentally dazed, stimulated, and very weak. The pulse rate was 132 beats each minute; the blood pressure in millimeters of mercury was 140 systolic and 70 diastolic. The basal metabolic rate was +82. The thyroid gland was enlarged bilaterally, with bruit over all poles. Pelvic examination revealed a 3 to 4 months' pregnancy. She was hospitalized but remained restless and irrational in spite of all treatment until February 15, when she became quiet and mentally more clear. Basal metabolic rate March 5 was +47. She was allowed to return home with instructions to take compound solution of iodine.

The patient returned April 14 with a basal metabolic rate of +72 per cent. Two injections of hot water were given into the thyroid gland, and April 24 the superior thyroid vessels on both sides were divided and ligated. Recovery was uneventful.

The patient returned October 19. She had had a premature delivery at home May 16, without complications. Her general condition had improved somewhat although weight continued to decrease. The thyroid gland was still large. The basal metabolic rate was +65 per cent; the blood pressure was 160 systolic and 88 diastolic. The pulse rate was 120. October 27, the right lobe of the thyroid gland was resected. The pathologist reported a few small, hæmorrhagic, fibrous, cystic, degenerating, colloid and fetal adenomata in a hypertrophic, parenchymatous gland. October 27, the patient's heart was fibrillating rapidly and she was irrational and coughing continuously. Pneumonia developed in the base of the left lung October 30, and death occurred 2 days later.

At postmortem examination, in addition to a large left lobe of the thyroid gland which still remained (weight 150 grams) and rather marked atrophy of the liver both grossly and microscopically, a rounded nodule was found buried in the right ovary. This measured 6 millimeters in diameter, was dark red on its cut surface with a fibrous capsule surrounding it (Fig. 7). The ovary appeared otherwise normal except for numerous cortical cysts. The left ovary also contained numerous small cysts, but no similar nodules. Microscopic study of the nodule from the right ovary revealed a tumor made up of typical adult thyroid tissue containing a thin colloid substance. At one edge of the nodule, definite evidences of hyperplasia were noted (Fig. 8). A fibrous capsule surrounded the nodule on all sides, cutting it off completely from the surrounding ovarian stroma. One small group of cells at the periphery adjacent to the capsule showed an atypical structure and remained unidentified, although the cells were suggestive of embryonic ependymal cells. The remainder of the thyroid gland (left lobe) was typical of the tissue under iodine treatment. The colloid was pale and few evidences of hyperplasia remained.

This case of frank hyperthyroidism is presented because of the small nodule of thyroid tissue in the right ovary. In this case, there is no doubt that the hyperthyroidism was due to hyperplasia of the thyroid gland itself. The interesting feature is the fact that the small nodule of thyroid tissue in the ovary also presented evidences of hyperplasia. The ovarian nodule showed more evidences of hyperplasia than the original portions removed from the thyroid gland. An additional interesting point is the small size (6 millimeters) of the nodule.

CASE 6. A woman, aged 43 years, presented herself at the clinic July 15, 1924, because of nervousness and short-

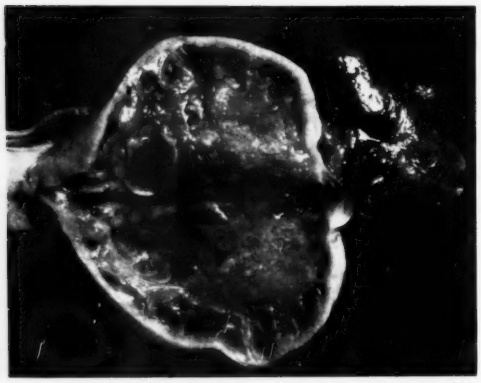

Fig. 7. Right ovary and tube. The ovary has been split longitudinally and laid open. To the left on the cut surface may be seen a dark rounded mass, which grossly and microscopically resembles thyroid tissue. Case 5.

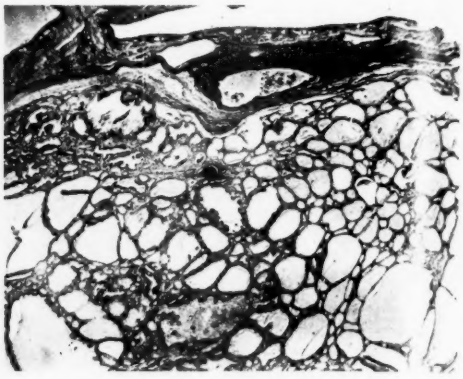

Fig. 8. Thyroid nodule (Fig. 7). Epithelial hyperplasia in some of the larger acini, and ovarian stroma with follicular cysts at the upper border of the section may be seen. Case 5.

ness of breath which had been present for several years. She also complained of tachycardia and palpitation, and had noticed slight tremor of the hands. There had been no increased sweating; she felt chilly rather than warm.

On examination the patient appeared to be stimulated. The pulse rate was 100 beats each minute. Multiple adenomata of the thyroid gland, enlarged myomatous uterus and a tumor about 7 centimeters in diameter in the position of the right ovary were found. It was decided that hyperthyroidism was not present and the metabolic rate was not determined. Exploration of the pelvis was advised, to be followed in several weeks by thyroidectomy.

At operation a degenerating myoma of the uterus and a cystic tumor of the right ovary were found, and removed. Pathological examination showed the right ovary to be replaced by a cystic mass measuring 8 by 7 centimeters and having a thick wall and a fatty, semisolid content without hair. Several small nodules were scattered over the inner surface of the cyst. These on cut surface were honeycombed with tiny cystic spaces filled with colloid material. Microscopic sections disclosed a thick, fibrous walled cyst lined by columnar epithelium in some areas, and broken up into irregular masses which were covered with columnar and cuboidal epithelium. The nodules mentioned were made up of thyroid-like acini filled with colloid. Marked hyperplasia of the acinar epithelium was seen in irregular areas. The cells were cuboidal or columnar with large, centrally placed nuclei and the acini in these areas were closely crowded together and small. Infiltration of the interstitial tissues was not seen and few mitotic figures were present.

Symptoms of nervousness, palpitation and tachycardia suggested hyperthyroidism in this case, but this was not substantiated by the entire clinical picture. The patient did not remain for the thyroidectomy, and was never heard from subsequently, so we do not know if the symptoms improved. The interesting feature of this case is the presence of very marked hyperplasia of the thyroid tissue in the ovary. The greater part of the tumor was made up of typical ovarian cystadenoma with nodules of the hyperplastic thyroid tissue scattered throughout. It seems possible that slight hyperthyroidism existed. Photomicrographs of this tumor are not presented because of the poor fixation of the tissues.

GENERAL COMMENT

Although many of the cases reported in the literature are definitely not cases of hyperthyroidism, there is present nevertheless, a potentiality for excess secretion of thyroid tissue. But just as large adenomatous goiters may not produce symptoms of hyperthyroidism, so a mass of thyroid tissue in the ovary may be present without causing hyperthyroidism. The iodine content of these tumors has been determined quantitatively by Meyer, King, and Norris and others and it has been suggested that an appreciable amount of iodine speaks for functional activity of the tissue. Outerbridge determined the presence of iodine qualitatively by Jones' differential staining method. Although iodine has been found in other organs such as muscles, suprarenal glands, thymus and spleen, it is said by Crotti to be present in the thyroid gland in larger quantities than in any other organ except the parathyroid glands. The iodine content of the thyroid gland varies with the age of the patient, and also with the iodine content of the diet. Ordtmann estimated the iodine content of the thyroid gland at approximately 0.1 per cent.

The iodine content of three of the tumors in this series was determined. The large tumor in Case 1 contained 0.105 per cent of iodine, dry weight.

The tumor in Case 4 contained 0.011 per cent of iodine, dry weight, and that in Case 3 contained 0.031 per cent, dry weight. The tissues had been fixed in formalin solution and it is probable that a considerable proportion of the iodine had been dissolved by the solution. An appreciable amount of iodine was found in the three tumors examined, greatest in the case of the large tumor in Case 1. This patient had had mild hyperthyroidism, and it is possible that the iodine she received accounts for the greater concentration of iodine in the tumor. In Cases 3 and 4, iodine had not been given. The thyroid tissue in the tumor in Case 3 contained the least amount of iodine and also the least hyperplasia of the epithelium.

The question of malignant change in these tumors has been of interest to the clinician and surgeon. Certain observers believe that tumors consisting entirely of thyroid tissue are all potentially malignant because they have overgrown all other tissue elements. From the cases reported in the literature as well as from our own cases, there seems to be little evidence of malignancy. It is Ewing's belief that some solid carcinomata of the ovary may be derivatives of teratoid thyroid tissue. Certainly, the majority of cases are neither clinically nor pathologically malignant. In Case 2, removal of the tumor afforded complete relief of all symptoms, and ascites did not return. In Case 1, which later came to necropsy, there was no evidence of metastasis from the tumor, death having been due to diffuse venous thrombosis of the portal system and elsewhere. Similarly in many cases from the literature the patients recovered completely after removal of the tumor. However, a few definitely malignant cases have been reported by Katsurada, Norris, Proescher and Roddy, Polano, and others. Ulesko-Stroganowa reported the only bilateral tumor of thyroid tissue of the ovaries on record. Although histological evidences of malignancy were not present, she believed that the bilaterality of the tumor was evidence of metastasis from one ovary to the other.

The not infrequent occurrence of ascites with these tumors has been of clinical interest although apparently of no prognostic significance. In Cases 2 and 4 the ascites showed no tendency to recur after operation, whereas in Case 1, although the rapidly accumulating fluid was at first thought to be evidence of malignancy, it could not be found at operation. This was later confirmed at necropsy. In Case 6, in which there was marked evidences of hyperplasia, ascites was not present. Frank has observed ascites in about 50 per cent of these tumors, and cases without ascites have been reported since he made this observation; his figure, therefore, seems far too high. Warren stated that 7.9 per cent of ovarian cystomata are associated with ascites, and it would seem that similar causes probably operate to produce ascites with ovarian tumors of various types and that therefore this figure (7.9 per cent) is a better estimate than 50 per cent. The presence of ascites is obviously not necessarily indicative of malignancy.

SUMMARY AND CONCLUSIONS

Cases of ovarian tumor containing large amounts of thyroid tissue are presented. In one case the ovarian tumor contained nodules of hyperplastic thyroid tissue.

Tumors of thyroid tissue in the ovary are probably of the nature of teratomata.

Since these tumors are of thyroid tissue, they are potential sources of thyroxin and in some cases seem to produce hyperthyroidism.

Three of the tumors were analyzed for iodine and an appreciable amount was found.

Hyperplasia of the thyroid epithelium, in varying degrees is commonly observed in these tumors.

Malignant changes were not observed in the tumors reported in this series.

Ascites is not infrequently an accompaniment of these tumors.

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COMPOUND INTRA-UTERINE AND EXTRA-UTERINE (LITHOPEDION) PREGNANCY

P. BROOKE BLAND, M.D., F.A.C.S., LEOPOLD GOLDSTEIN, M.D., AND WILLIAM W. BOLTON, M.D.,
PHILADELPHIA
From the Department of Obstetrics, Jefferson Medical College Hospital

CALCIFIED fetuses or lithopedions have been recognized for centuries and have been reported from time to time in the literature. The earliest cases on record, according to Dorland, are those of Venetiss, 1595, Albosius, 1597, and Densingeus, 1661. In 1881, Kuechenmeister collected 45 cases of various forms of fetal calcification recorded during the 200 year period antedating 1880.

Lithopedions have occasionally been discovered during the performance of operations for various pelvic neoplasms and they are sometimes discovered accidentally at autopsy. In many instances, it has been observed, that patients have successfully passed through one or more full term pregnancies, with birth of healthy children, without the extrinsic gestation giving rise to difficulty.

In exceptional instances, the presence of an extra-uterine fetal mass is discovered during the course of a normal intra-uterine gestation, as in the case recently reported by Balaban, and as in the case presented in this paper.

In many of the cases recorded, the ectopic pregnancy has antedated the intra-uterine impregnation by many years. As in the case history herewith presented, patients are ofttimes entirely unaware of any abnormal abdominal condition, the extra-uterine fetus not causing the mildest discomfort.

Since the publication of Kuechenmeister's exhaustive monograph on lithopedions, a long list of cases of this rather extraordinary condition has been recorded in the literature.

Masson and Simon, in 1928, assembled and published a summarization of the cases recorded from 1582 to 1926. This comprised in the aggregate 174 cases. To this number they added the records of nine lithopedions observed in the Mayo Clinic during a period of 24 years, from 1903 to 1926, inclusive. The addition of these cases make a grand total up to 1926, of 183.

In a perusal of the literature since that date, we found the records of 13 additional cases (Table I). These were not reported by the writers already mentioned, nor had they been referred to subsequently as a collection. These cases with the one herein described make an aggregate of 197.

Here it may be of interest to mention that in 1906, one of us (Bland) reported a case of a mummified fetus which was carried by the patient for a period of 15 years. The structure was removed through an abdominal incision. Dissection of the mass after extirpation disclosed that it had probably reached the eighth month of development. During the 15 years, the patient has passed successfully through three full term pregnancies.

TYPES OF LITHOPEDIONS

Kuechenmeister developed a hypothesis in an effort to explain the formation of calcified fetuses and classified the different types of this anomaly according to the degree and location of the process as follows:

1. *Lithokelyphos.* In this type, calcification and fatty degeneration occur in the exudative lymph surrounding the fetal membranes and in the membranes themselves. As a result a stone-like capsule is formed about the fetus, while the fetus itself may undergo slight or massive degenerative changes.

2. *Lithokelyphopedion.* This is a form in which the fetus becomes adherent to the sac, with both the fetus and sac showing widespread infiltration with lime salts. Kuechenmeister believed that this variety resulted when the amniotic fluid escaped or was absorbed, with the membranes themselves becoming tightly wrapped around the fetus.

3. *Lithopedion* (*stone child or lithotecnon*). This includes in general all types of calcified fetuses, although the term refers especially to the form in which the fetus itself undergoes organization and massive calcification. A true lithopedion forms when the fetus escapes unattached into the peritoneal cavity with or without the enveloping membranes.

Depending on the duration of the gestation outside of the uterus, various changes inevitably take place in the fetal structures. Chemical alteration, such as saponification, and a drying process, mummification, frequently occur. After a time, lime salts are deposited in the fetal tissues or in the membranes, with the result that stone-like masses are finally produced. With these

Fig. 1. Roentgenogram of abdomen showing skeleton of viable fetus in the left side and lithopedion in the right side.

phenomena present, a fetus is designated a lithopedion.

It has been demonstrated that when mummification of an extra-uterine fetus occurs, no trace of the placenta or placental tissue can be found. Mummification results from the absorption of fluids, whereupon the remaining soft parts are converted into hard, parchment-like material.

COMPOUND INTRA-UTERINE AND EXTRA-UTERINE PREGNANCY

The synchronous occurrence of an intra-uterine pregnancy with an ectopic lithopedion is not often encountered. An advanced extra-uterine gestation is usually discovered and surgically removed before lithopedion formation or calcification takes place. Occasionally an advanced gestation outside of the uterus becomes either mummified or calcified. Under such circumstances, the patient may become impregnated once or repeatedly and be delivered normally at term. During this time the old extra-uterine pregnancy may escape detection. On the other hand, it may be discovered during the course of an intra-uterine pregnancy. The designation of compound pregnancy describes this combination of affairs, namely, an intra-uterine gestation associated with a long standing mummified or calcified fetus in the abdominal cavity.

TABLE I.—SUMMARY OF THIRTEEN CASES OF LITHOPEDION REPORTED IN THE LITERATURE

Author	Date of report	Features of case
1. Saenger	1925	Patient 57 years old with carcinoma of fundus; lithopedion behind uterus probably of 32 years' duration, having origin in tubal abortion
2. Krauss	1925	Lithopedion found at autopsy of 8 year old woman, who had had an extra-uterine pregnancy 40 years previously
3. Ewers	1925	Intra-uterine pregnancy complicated by lithopedion remaining after ourious labor 3 years previously
4. Abernathy	1927	Details not obtained
5. Balaban	1929	Patient 31 years old had lithopedion for 8 years, during which time she had two normal pregnancies. Lithopedion discovered by X-ray examination during course of another pregnancy which terminated normally. Operation was refused
6. Butler	1929	Patient, age 34, operated upon 3 years previous to roentgen study for ruptured ectopic pregnancy, at which time the fetus was not recovered. X-ray examination revealed small calcified fetus in upper right quadrant, and it was successfully removed
7. Das	1930	Patient aged 35 years. Full term lithopedion retained for 2 years and successfully removed
8. Watters	1931	Patient, age 34, carried mummified tubal fetus for 11 years, during which period she gave birth to 3 full term children. Lithopedion was successfully removed
9. Goodwin	1931	Patient, age 32, passed through a "mock" labor and later had periods. X-ray examination showed extra-uterine fetus with areas of calcification. No symptoms. Lithopedion weighing 10 pounds removed
10. Engels	1931	Calcified lithopedion of 4 years' duration in one tube with a recent pregnancy in the other tube. Surgical removal
11. Grimm	1931	Lithopedic mass of 16 years' duration, diagnosed by the roentgen-ray, removed surgically
12. Villarreal	1931	Lithopedion of 7 months' development carried for 8 years, and removed successfully. One normal pregnancy in the interval
13. Sante and Emmert	1932	Extra-uterine full term fetus diagnosed by X-ray and studied roentgenologically throughout its course of lithopedion formation for 8 years

COMBINED INTRA-UTERINE AND EXTRA-UTERINE PREGNANCY

At this point it is of interest to mention that not infrequently an intra-uterine gestation commences almost synchronously with an extra-uterine one. The first case of combined intra-uterine and extra-uterine pregnancy, according to Novak, was recorded by Duverney in 1708, who discovered the condition at autop-

Fig. 2. Photograph of lithopedion. The mass weighed 2 pounds and 10 ounces and measured 15 centimeters in length, 10 centimeters in width, and 7.5 centimeters in depth.

Fig. 3. Roentgenogram of lithopedion after its removal.

Neugebauer in two exhaustive contributions collected 244 cases of combined intra-uterine and extra-uterine gestation occurring in a period of more than 200 years (1708 to 1913). Novak found 32 additional cases of combined pregnancy of this type in the literature from 1913 to 1926. With the 2 cases which he personally observed, the total reaches 278. In 1927, Bermann reported a pregnancy of 5½ months complicated by extra-uterine gestation and dermoid cyst, which brings the total to 279 cases.

A CASE OF ADVANCED INTRA-UTERINE PREGNANCY ASSOCIATED WITH ECTOPIC GESTATION OF LONG STANDING

Q. S., colored, age 25 years, registered at the prenatal clinic of the Jefferson Medical College Hospital, on November 13, 1931. Her general health had always been good. She gave no history of previous operations. The menstrual epoch commenced at the age of 15; the cycle was of the 28 day type and was always normal. The last normal period occurred in the "middle" of May, 1931.

The patient had had two full term normal pregnancies, and the children were recorded as being 11 and 13 years of age respectively. There was no history of missed periods or abortions. She felt well throughout the period of gestation and did not manifest symptoms of any kind.

Examination in the antenatal clinic revealed a fairly well developed colored woman exhibiting all the physical signs of pregnancy. The abdomen was enlarged to the size of a 7½ months gestation. In the right side of the abdomen, on a level with the umbilicus, a large mass, the size of a grapefruit, was felt. The tumor was not tender and on palpation it imparted a crackling sensation. The mass seemed to be external to the enlarged uterus and separate from it.

The patient was admitted to the maternity ward for radiologic examination and further study.

Laboratory findings: Wassermann and Kahn tests were negative. The blood count showed red blood cells, 3,750,000; white blood cells, 8,000; hæmoglobin, 70 per cent. Urinalysis was negative, except for 30 to 40 white blood cells, per low power field.

Roentgenological findings: Pyelography was included in the roentgen examination because of the presence of many leucocytes in the urine. Radiographic examination disclosed that the right renal pelvis and calyces filled normally with sodium iodide and that structurally the kidney was normal. The skeletal outlines of two fetuses could readily be made out. The fetus occupying the left side of the abdomen was viable, whereas the one on the right side showed overlapping of the cranial bones and apparently had been dead for some time. The head of the living fetus was directed toward the maternal pelvis, the back to the left of the maternal spine and anteriorly (L.O.A.). There was no evidence of disproportion between this fetus and the maternal pelvis. The fetus in the right half of the abdomen was encapsulated and much smaller than the viable one (Fig. 1).

The ureteral catheter was deviated slightly to the right in the pelvis, due to the presence of the fetal head. It passed up the ureter between the non-viable fetus and the viable one.

The plates of the skull of the non-viable fetus showed extreme overlapping, indicating that it probably had died at least several months previously. On palpation over the right half of the abdomen, there was an area of crepitation coinciding with the skull of the dead fetus. The crepitation seemed to be associated with the motion of the fetus on palpation.

The non-viable fetus was believed to be extra-uterine because the outline of the shadow of the uterus could be

seen, while that of the fetus fell to the right of it. There seemed to be considerable calcification of the membrane around the fetus.

From the radiographic findings the following diagnosis was made: intra-uterine pregnancy (L.O.A.); extra-uterine pregnancy with dead fetus (lithopedion).

Treatment: On December 3, 1931, a laparotomy was performed under general anæsthesia. An encapsulated tumor, about the size of a grapefruit (Fig. 2), which sprang from the right tube and was bound down to the cæcum, was found. It was removed together with the tube and ovary. On the third day following the operation, after a short, easy labor, the patient delivered a stillborn, premature fetus spontaneously. Convalescence was entirely uneventful, the abdominal incision healing by primary union. Patient discharged in good condition December 23.

Description of lithopedion: The hard irregular mass (Fig. 2), weighing 2 pounds and 10 ounces, measures 15 centimeters in length, 10 centimeters in width, and 7.5 centimeters in depth. It is completely enveloped by a thick, gray, fibrous capsule to which a small ovary is attached. In several areas the skeletal structure can be distinctly palpated and the forms of the extremities are easily discernible through the sac. The hard, fibrous sac enclosing the fetus was probably formed from the amniotic membranes which had become infiltrated with lime salts.

A crackling sensation is imparted by the mass to the fingers and especially by the bony plates of the skull. When the indurated capsule was incised, decomposing bones and tissue protruded. Several small bones had undergone such decomposition that they dropped out when the capsule was incised.

From the appearance of the bones, it would appear that the fetus had reached 7 or 8 months' development before death had taken place. As the specimen was not dissected, it is impossible to state the character of preservation of the innermost contents.

Figure 3 is roentgenogram of lithopedion after removal.

The case of lithopedion described herewith illustrates the importance of careful routine antenatal examination. Only by such procedure is it possible to minimize the danger of inadvertently overlooking abnormal conditions which ordinarily do not give rise to special subjective symptoms.

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ELECTROCOAGULATION OF THE MELANOMA AND ITS DANGERS

PHILIP D. AMADON, M.D., MONROE, MICHIGAN

A SERIES of 27 cases of melanoblastoma of the skin was reported a short time ago[1] at which time one was disappointingly impressed with the failure of our existing methods of treatment. The treatment of these melanotic growths by the popular use of the "electric needle" disclosed several facts which led to this study. In the series studied, those cases treated by electrocoagulation showed a 100 per cent recurrence at the site of the primary, with early regional and generalized metastasis in the majority of cases. The untreated melanoblastoma progressed less rapidly to local and general metastasis than those electrocoagulated. The average time for the appearance of regional metastasis in the cases so treated was $5\frac{1}{7}$ months and $11\frac{1}{2}$ months for generalized metastasis.

The term melanoma, which specifies the character of the tumor cell containing a variable amount of an iron-free pigment, melanin, will be used in an endeavor to show no partiality as to the connective tissue, epithelial or endothelial origin of these growths.

The malignant melanoma has its origin as a rule from the nævus cells of pigmented warts and moles. The benign melanoma or pigmented nævus consists essentially of a localized area of pigmented basal cells, with the presence of so called "nævus" cells arranged in groups or columns in the upper corium.

In the study of this problem the following observations were made permitting of possible explanation of the facts and presenting an application to the entire field of electrosurgery of malignancy.

A more complete understanding of the changes taking place may be possible if a review of the mode of metastasis of the malignant melanoblastoma is made. The lymphatics of the skin are collected from very fine capillaries in the epidermis in lymphatic trunks in the fascial planes, which eventually terminate in the regional lymph nodes. It has been shown by Campbell de Morgan and later by Handley that the growth of melanoblastoma occurs first along the lymphatics. Figure 1 demonstrates the mechanical permeation of the lymphatics in the corium, *E;* and in the fascial plexus, *C;* the spread of the tumor cells occurring along the line of least resistance. Handley, after extensive investigation, has described three zones surrounding the primary lesion. Farthest from the lesion in the fascial lymphatic plexus only (Zone I) with no invasion of the surrounding tissues are found the tumor cells entirely within the walls of the lymphatic vessels, *C.* Within this zone is an area of inflammatory reaction (Zone II) with perilymphatic leucocytosis and fibrosis due to rupture of distended lymphatics of the fascial plexus with melanotic tumor cells with a retrograde permeation of the subepithelial tributary lymphatics toward the skin, *E* and invasion of the fascia and muscles. Nearest the primary growth is a zone (Zone III) in which all of the permeated lymphatics have become strangulated by the perilymphatic fibrosis incident to the inflammatory reaction set up by the presence of the tumor cell and, as a result, the lymphatics have entirely disappeared, thus leaving only isolated large nodules of malignant cells (*II-J*), increasing in size and invading the neighboring vessels, both veins and arteries. That blood vessel dissemination occurs secondarily to lymphatic permeation is thus clearly shown. It is seen that the process is entirely mechanical, the tumor cells spreading most widely in the larger, deeper lymphatics and invading the corium and epidermis only after the inflammatory process set up by their presence has been sufficient to fibrose and choke the deeper lymphatics.

A group of benign skin lesions was carefully selected in studying the changes taking place in the skin and subcutaneous tissues on electrocoagulation in the hope that while dealing with a benign lesion, sufficient changes might be safely observed and application made to the malignant lesions.

A group of senile keratotic lesions were treated with the electric desiccating needle. In this series so treated, many of the lesions were surrounded by dilated venules which extended from the lesion for several centimeters in normal tissue. It was in this particular group that the observations were made. Definite changes, visible to the naked eye took place. On application of the desiccating or coagulating needle to the central portion of the lesion, globules and bubbles appeared in the deeper portions and at the periphery. As the process proceeded, a venule at the periphery would suddenly dilate to twice its normal size and blanch free from blood, beginning at the proximal end nearest the lesion and extending to its most

[1] J. Michigan State M. Soc., Oct. 1930.

Fig. 1. *A*, Epidermis with primary melanoma *G*; *B*, corium with blood vessels *F* and superficial lymphatics *E*; *C*, fascial lymphatic trunk; *D*, muscle. Zone I is furthest from the primary lesion, the melanotic cells are entirely within fascial plexus *C*. Zone II—fewer melanotic cells are present within fascial plexus; perilymphatic leucocytosis *I* and fibrosis of lymphatics; permeation of superficial lymphatics *E* toward epidermis in corium and in muscle. Zone III is nearest the primary lesion. There is complete fibrosis of the fascial lymphatic plexus; invasion of vessels *J* with melanotic cells; groups of melanotic nodules *H* free in corium and muscle.

Fig. 2. Senile keratotic skin lesion with surrounding visible dilated venules.

distal part. This same phenomenon could be made to occur in each of the peripheral, visible venules by continuing the coagulation. In several instances the escaping globules of tissue steam or gas would suddenly fill the venule and express the blood to its distal end, only to dilate the vessel to still greater size as the coagulation continued. Figures 2 and 3 illustrate the appearance of the lesion and dilated venules surrounding, both before and following electrocoagulation. Thus was demonstrated the mechanical passage of tissue gases, generated by electrocoagulation, into the visible venules surrounding the lesion.

That such a phenomenon occurs not only in the visible venules but also in the deeper vessels and lymphatics can hardly be denied. The application of this observation to the use of the electric needle in the treatment not only of malignant melanoma but to malignancy in general thus becomes appalling.

With the peculiar lymphatic metastasis heretofore described and so ably demonstrated by Handley; the mechanical passage of the tumor cells along the line of least lymphatic resistance and secondarily by direct extension into the blood stream; the result of electrocoagulation can be readily appreciated. The tissue gas bubbles generated during the process, which are forced under apparent pressure into the surrounding lymphatics and vessels, carry before them the unstable malignant cells; which without this assistance are already passing widely along the lymphatics, and thus force the invasion to even greater dimensions.

In referring to Figure 1 in which the three zones surrounding the skin lesion are demonstrated, it is seen that the malignant cells are farthest removed from the primary lesion in the fascial lymphatic trunk *C*. Actually to state the actual dimensions of Zones I, II, and III and with any degree of certainty determine the definite extent of progress in the fascial plexus of Zone I is impossible because of the varying grades of malignancy, duration, and treatment.

In reviewing the cases treated by electrocoagulation, one is confronted with a large number in which the skin lesion itself has been attacked. In another group the electric needle has first been passed through apparently healthy tissue at varying distances from the primary lesion, completely encircling the lesion before its actual coagulation. The explanation of the second procedure being to seal off the lymphatics before attacking the primary. In both groups the recurrence was 100 per cent.

An explanation of the same degree of recurrence in the group in which the lesion is first completely encircled through apparently healthy tissue is now possible of explanation. Although the process has been carried through apparently healthy tissue on the basis of being wide of visible superfical lesion the malignant cells are present in the fascial plexus at greater distances, even in many instances to the nearest group of lymph nodes. While the lesion is being surrounded by the needle the tissue gas is generated in exactly the same manner as in coagulating the primary lesion and when the fascial plexus is encountered the bubbles escape into that avenue and force before them the malignant cells present to an even wider extent.

Reference to Figure 4 again illustrates the three zones surrounding the primary growth. Figure 4 illustrates diagrammatically what occurs by the generated tissue gas in forcing the malignant cells wider when the lesion is encircled through apparently healthy tissue.

Thus far the discussion has dealt only with the treatment by electrocoagulation of these mel-

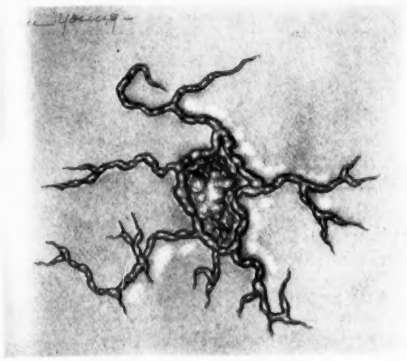

Fig. 3. Senile keratotic lesion seen in Figure 2 following electrocoagulation, demonstrating the dilatation of the venules by tissue steam.

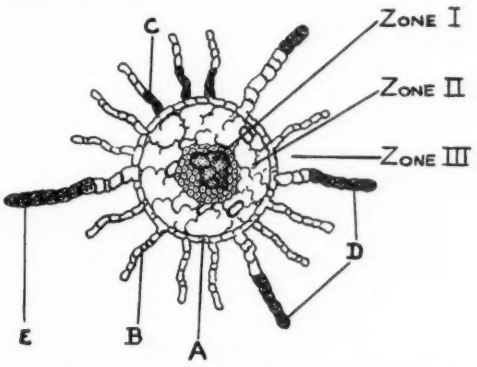

Fig. 4. *A*, Site of electrocoagulation by encircling primary growth; *B*, subfascial lymphatics containing no tumor cells; *C*, fascial lymphatic containing tumor cells in Zone II; *D*, fascial lymphatics dilated with tissue gas from electrocoagulation; *E*, tumor cells forced beyond Zone II by pressure of tissue gas in fascial lymphatics.

anoma which are known to be malignant. That a sufficiently large group of benign melanoma of the skin exist which show malignant change following treatment with the electric needle is not denied, although the difficulties arising in determining the actual percentage is wellnigh impossible. Of the 27 cases in this series, the mole was present in 21. In a previous paper the writer endeavored to show that moles, birthmarks, and warts of congenital origin may remain benign and unnoticed for years only to undergo malignant changes later, thus presupposing an exciting factor. Undoubtedly, this factor in the majority of cases arises as chronic irritation. Some writers regard the melanin pigment in the light of a chemical irritant which may first produce an abnormal epidermal cell proliferation. Borst and others hold that it is set free in the tissue spaces and initiates a malignant proliferation in the endothelial and connective tissue cells. That the presence of a congenital nævus or birth mark is not essential in the production of a malignant melanoma is evidenced by the reported cases of the development of malignant melanoma arising in the puncture wounds, e.g., from a thorn in the foot, especially in the races of the upper Nile. The writer reported a case of malignant melanoma arising in the puncture wound on the leg of a paper hanger as a result of pricking the leg with the points of his scissors carried at the side. Handley explains this as being due to the traumatic implantation into the subcutaneous tissue of a group of dermal connective tissue cells; of actual or potential chromatophores.

It seems reasonable to conclude that the improper coagulation of benign skin lesions with the electric needle acts not only as an acute irritant in stimulating cells to malignant change, but also sets free the abundant melanin present in the tissue spaces where it acts as a chemical irritant, according to Borst, and traumatically implants into the subcutaneous tissue the actual chromatophores, according to Handley, thus causing malignant change.

Until some future time, when a better method of treatment for this most malignant of diseases is advanced, surgical excision, with due respect to the anatomical disposition of the lymphatics and thorough knowledge of the spread of the neoplastic cells, should remain the procedure of choice. A wide circular or elliptical incision should be made through healthy tissue far removed from the primary growth. The surrounding skin should be elevated or undercut as far as possible and the subcutaneous fat and fascia incised at the extreme base of the undercut skin in a circular manner down to the underlying muscle. The entire mass of primary growth, subcutaneous fat and fascia, with a thin portion of underlying muscle, is then removed by a sharp dissection. Greater assurance is then obtained by removing the gland draining area in the same aforedescribed fashion.

SUMMARY

1. The cases of malignant melanoma in a series of 27 cases treated with the electric needle showed a 100 per cent recurrence.

2. Electrocoagulation of a group of senile keratotic lesions demonstrated the escape of "tissue gas" into the peripheral visible venules under pressure.

3. An application of this discovery to electrocoagulation of malignant melanoma renders plausible the explanation of high recurrence on the basis of the mechanical forcing of unstable malignant cells more widely into the tissues by pressure exerted in the lymphatics and vessels by generated "tissue gas."

4. Preliminary encircling of the primary growth with the electric needle through apparently healthy tissue is unsound as the fascial lymphatics wide of the primary lesion may be filled with tumor cells, the same phenomenon of generated "tissue gas" pressure occurring here with similar results.

5. Inefficient treatment of benign skin lesions, especially the benign melanoma with the electric needle, may initiate malignant change by acting as an irritant or by the implantation of potential chromatophores into the subcutaneous tissue.

6. Surgical excision of these lesions with special reference to the anatomy and mode of metastasis, remains the procedure of choice.

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A CONTINUOUS FIGURE-OF-EIGHT SUTURE FOR MUSCULAR AND PERITONEAL APPROXIMATION IN CÆSAREAN SECTION

FREDERICK C. IRVING, M.D., F.A.C.S., BOSTON, MASSACHUSETTS

WHEN closing the uterine wound in cæsarean section practically all operators use first a continuous stitch which unites the innermost fibers of the muscularis and avoids the mucosa. This suture line is shown in Figure 1. The closure of the remainder of the uterine wall so as to secure accurate coaptation and hæmostasis without constriction of tissue has always been a problem. The difficulty is increased when the uterine wall is unusually thick. I have in the past employed for this purpose one or more layers of interrupted single, or of continuous or single figure-of-eight sutures according to the nature of the case. It has been found, however, that none of these methods was ideal, or that none would produce even approximately the desired effect in every case. To overcome these objections I have of late been using a continuous figure-of-eight suture which seems to solve the difficulty in a satisfactory manner. It unites at the same time the middle portion of the muscularis and the superficial muscle fibers along with the serosa and secures good approximation and hæmostasis. Because of the length of the suture, which makes for elasticity, and the absence of knots except at the two ends, there is no constriction of tissue.

While designed primarily for the classical cæsarean section it may be used equally well in closing a vertical incision in the lower segment. In the latter case one begins at the lower angle of the wound where the uterine wall is thin with an over and over stitch which is continued upward until the thicker portion is reached, when the figure-of-eight is begun.

Three-quarters of a length of chromic catgut is threaded on a round pointed curved needle, but is not tied in or rethreaded. Beginning at one angle of the wound the suture is passed through the intermediate zone of the muscularis on either side and tied, thus anchoring the stitch. The needle is then reversed in the needle holder and passed from within the wound outward on one side through the superficial muscularis and peritoneum. Still keeping the needle reversed the suture is passed through the peritoneum and superficial muscularis of the opposite side into the wound. As the stitch is tightened, it closes the peritoneum and buries the first knot. The needle is then placed in the usual position in the needle holder. Bites are taken in the deeper portions of the muscularis as before, the needle is again reversed and the outer portion of the wound united

Fig. 1.

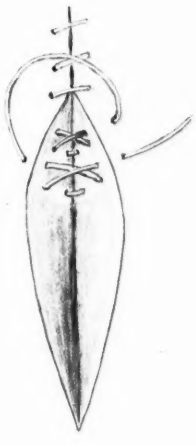

Fig. 2.

Fig. 3.

Fig. 4.

Fig. 1. Suture line; Fig. 2. Detail of suture. Fig. 3. Taking last superficial stitch. Fig. 4. The suture has been cut, the end dropped into the wound, and final knot buried.

as described (Fig. 2). These maneuvers are continued until the last deep stitch has been taken and the final superficial loop is about to be placed. At this point as the needle is passed from within outward the assistant grasps the free end of catgut and draws it taut. The needle is then passed from without inward, making the last superficial stitch one of double suture material (Fig. 3). The suture is now tied and cut and its end falls into the wound, leaving the final knot also buried (Fig. 4).

Although I have seen no reference to this method of suture it is possible that it has been used and described before. Should that be the case, I would gladly surrender priority to anyone who wishes to claim it.

BRANCHIAL AND THYROGLOSSAL DUCT CYSTS AND FISTULAS IN CHILDREN

CONRAD J. BAUMGARTNER, M.D., Los Angeles, California
From the Childrens Hospital, Los Angeles

THE clinical picture of branchial and thyroglossal duct cysts and fistulas is frequently unrecognized. Particularly is this true in children when the cysts and fistulas are so often mistaken for abscesses or broken-down lymph glands, and are repeatedly incised and drained without effecting a cure. Although many are not manifest until later years, probably the greater majority of branchial and thyroglossal duct fistulas and cysts that do occur in children are not properly treated until adult life.

EMBRYOLOGY

Noteworthy studies of the embryology of the branchial apparatus have been made by Rathke, His, Born, and others. Undoubtedly the greatest single contribution is that of Wenglowski, who, in 1912, published a monograph in which he gave the findings of detailed study of serial sections of a large number of human embryos beginning with 2 millimeters and ending with 49 millimeters. I shall first briefly outline the embryology according to Wenglowski and then deal with the clinical side of the subjects.

During the second week of embryonic life, certain changes take place in the fetal foregut (Fig. 1): From the interior lateral walls of entoderm, five outpouchings or diverticula appear. These are called pharyngeal pouches. Simultaneously the external ectoderm becomes indented over the corresponding pharyngeal pouches. These are the branchial or outer pharyngeal grooves. As the small grooves approach the pouches, the mesoderm is pushed aside so that for a time ectoderm and entoderm come into contact. The contacting areas are the closing membranes which in gill-bearing animals disappear forming the gill clefts, opening from the pharynx to the exterior. Such perforation, of course, does not normally occur in birds and mammals.

The grooves and pouches thus formed separate a series of rounded bars of mesoderm which has been pushed aside by them. These are termed branchial or visceral arches, of which there are 6, all meeting ventrally in the midline of the neck. In each arch there is developed a cartilaginous bar consisting of a right and left half, and in each bar also is the anlage of one of the primitive aortic arches.

The first arch is called the mandibular arch, and from it are developed the lower lip, the mandible, the muscles of mastication, and the anterior part of the tongue. Its cartilaginous bar forms the incus, malleus, and a portion of the mandible.

The second is the hyoid arch. It gives origin to the structures of the upper part of the neck. From its cartilage are developed the styloid process, stylohyoid ligament, and lesser cornu of the hyoid bone. The first two arches grow more rapidly than the remainder so that the latter four become telescoped, the first two arches leaving a deep depression, the cervical sinus. (Wenglowski claims that the third arch telescopes to form the sinus.) The ventral ends of the second, along with those of the third arch, assist in formation of the body of the hyoid bone and the posterior part of the tongue. The third arch assists in the formation of the sides of the neck and its cartilage gives origin to the greater cornu of the hyoid. The fourth and fifth arches also assist in forming the sides of the neck, while the ventral portions of their cartilages unite to form the thyroid cartilage. The sixth arch gives origin to the cricoid, arytenoid, and tracheal cartilage.

From the first external indentation, the first branchial groove, arise portions of the auricle and external acoustic meatus, while of the second, third and fourth grooves, no traces persist.

From the first internal outpouching, first branchial pouch, are formed the auditory tube and tympanic cavity, the tympanic membrane arising directly from the closing membrane between the first and second arch. In the second pouch lies the anlage of the tonsil. Wenglowski demonstrated that from the third pouch on either side, a small duct, the thymic duct, descends into the mediastinum to form the thymus. This duct passes in the general direction of the sternomastoid muscle, laterally to the thyroid, and is lined with squamous epithelium surrounded by lymphocytes. He likewise demonstrated remnants of this tubule in adult necropsy dissections. From the fourth pouch a comparatively short tubule passes on either side in a somewhat medial direction to form the lateral lobes of the thyroid. The parathyroids likewise originate in this pouch. The fifth pouch gives origin to the ultimo branchial bodies, which, although enveloped by thyroid tissue, leave no identity in the human adult.

During the third week a rounded swelling or bud appears on the ventral side of the foregut just behind the first arch. This is the tuberculum impar which, along with two similar swellings appearing laterally, form the anlage of the buccal part of the tongue. A V shaped swelling arising somewhat posteriorly is called the copula and is the anlage of the posterior part of the tongue. In the fourth week, a diverticulum descends between the tuberculum impar and copula, and passes as a tubular duct downward, anteriorly to the trachea, to form the middle lobe of the thyroid gland. The point of descent remains as a depression at the base of the adult tongue which is known as the foramen cæcum. The tubular structure is the thyroglossal duct. It later atrophies and is obliterated but occasionally remains patent, producing the congenital anomaly, thyroglossal duct cyst or fistula.

BRANCHIAL CYSTS AND FISTULAS

There are several theories regarding the evolution of branchial cysts and fistulas. (1) That they are caused by a vestigial remains of the branchial grooves or pouches. (2) That they are a result of an embryonic perforation of the closing membranes. (3) That they are a persistance of the cervical sinus formed by the telescoping of the rapidly growing first and second arches over the remaining arches. (4) That they are due to a remains of the thymic duct which descends from the third pharyngeal pouch as demonstrated by Wenglowski in 1912.

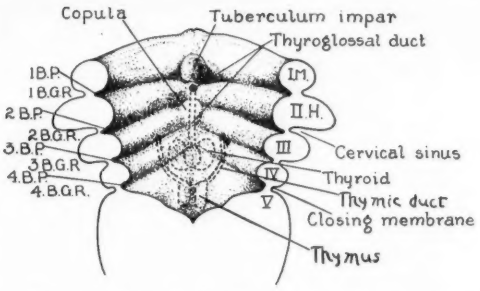

Fig. 1. Schematic drawing showing development of branchial apparatus. *I. M.*, Mandibular arch. *II. H.*, Hyoid arch. *III, IV, V*, Third, fourth, and fifth branchial arches. *1 B. P., 2 B. P., 3 B. P., 4 B. P.*, First, second, third and fourth branchial pouches. *1 B. G. R., 2 B. G. R., 3 B. G. R., 4 B. G. R.*, First, second, third, and fourth branchial grooves.

Clinical features. A distinction is frequently made between branchial cysts and fistulas and each spoken of as a distinct entity. It appears, however, that they are all simply a sinus tract which forms a cyst when the drainage is inadequate or obliterated. The lining of both cysts and fistulas consists of squamous epithelium surrounded by a cover of lymphoid tissue.

According to E. Wyllys Andrews, there are five types of branchial cysts or fistulas: (1) complete branchial fistula with internal and external opening; (2) incomplete external fistula, no internal opening; (3) incomplete internal fistula, no external opening; (4) branchial cysts, no internal or external opening; (5) branchial dermoid.

The surgical records of the Childrens Hospital show only 4 cases of branchial cysts and fistulas. This is, however, not a true index of the incidence of this anomaly. In 1929 Hyndman and Light reviewed a series of 90 cysts and fistulas. In their series the average age of onset was 17 years and the condition was noticed at birth in only 21 per cent, and only 11 occurred before the age of 11 years, which is the age limit of admission at the Childrens Hospital. The ages of these 4 children were 2, 2, 3, and 9 years, respectively. There were 2 each girls and boys. The sides of the neck involved were likewise equally represented. The age of onset of these children was, at birth, at 2 months, at 18 months, and at 7 years. In the cases reviewed by Hyndman and Light, 53 occurred in females and 47 in males, and of the 28 cysts, 35.5 per cent were on the right side and 64.5 per cent on the left, while of the 62 fistulas, 51.8 per cent were on the right, 31.4 per cent on

Fig. 2, left. Branchial cyst which developed after infection of a fistulous tract.

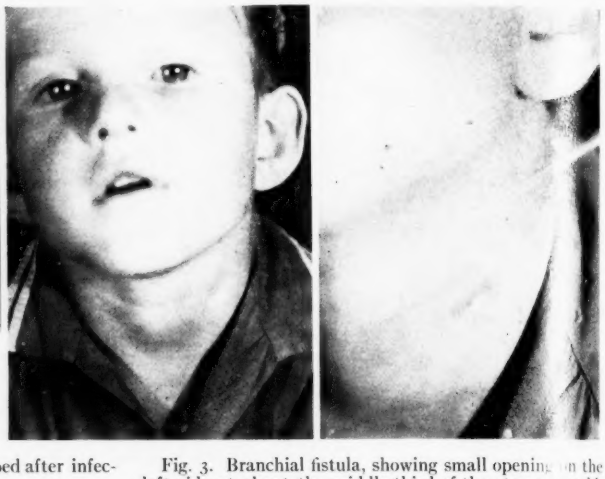

Fig. 3. Branchial fistula, showing small opening on the left side at about the middle third of the sternomastoid.

the left, and 16.8 per cent were bilateral. Multiple openings occurring on 1 side are, indeed, rare. There is but one reported by Virchow in 1861. Familial tendency is likewise not the rule, but again scattered cases have been reported. In Virchow's report of 1861, there is the occurrence in a mother and 8 children, and 2 other cases of family tendency, and in the 1929 study of Hyndman and Light, they reported cases in which the mother and 3 of her 5 children presented fistulas.

Clinically a branchial cyst usually manifests itself simply as a uniform, painless, nontranslucent, semifixed, fluctuant tumor, which is never tender except from pressure or secondary infection (Fig. 2). Ordinarily its presence does not cause the child any particular discomfort. There have, however, been reports of serious trouble caused by pressure on neighboring structures, particularly difficulty in breathing or swallowing. Thomson, of England, reported a branchial cyst which produced hoarseness and was accompanied by a fixed vocal cord. When the swelling was at its height, there was dysphagia and cough with complete misery of his patient. At exploration, the cyst was found attached to the larynx and passed to the lateral wall of the pharynx. The symptoms completely subsided after excision of the cyst. A branchial cyst has a uniformly characteristic position along the anterior border of the sternomastoid and extends under it to the deeper structures of the neck. The size depends upon the amount of drainage or secretion present and may vary from a centimeter in diameter to almost filling the entire side of the neck. The average size, however, is about that of a walnut.

The clinical picture of branchial fistula is that of a sinus which periodically drains a mucoid or thin milky material which may be associated with a cyst, depending upon adequacy of drainage. The fistula is also not prone to give any serious trouble in the average case except that the discharge is annoying to both parent and patient and the fistulous tract often stops drainage for a time with the production of a cyst which again periodically empties itself.

Not infrequently, however, repeated secondary infections do take place with an occasional serious cellutitis of the neck. Also some very aggravating conditions have been observed: A case reported by Louis Carp in 1926 is that of a boy 5 years of age, who, with a branchial fistula gave a history of an unproductive cough of 2 years' duration which was unsuccessfully treated by tonsillectomy and medical measures. At exploration an incomplete fistulous tract was found adherent to the vagus nerve. Excision of the tract brought about relief of all symptoms which were, as the author stated, quite surely due to vagal irritation. It is known that probing or pinching a tract has produced vagal symptoms such as cough, palpitation, intermittent pulse, hoarseness, pallor, and sweating. I have had occasion to operate on an 18 months old child whose mother said the baby had had asthmatic attacks whenever the fistulous tract stopped draining and became distended. This appeared to be undoubtedly a case similar to that reported by Carp. Furthermore, at operation

a distinct nerve fiber was found attached to the tract, extending deep to the carotid sheath, apparently leading to the vagus nerve. The child has, however, had several mild attacks since and has been found sensitive to milk.

The fistulous opening may be situated at any level of the neck but is constantly and without variation just anterior to the sternomastoid muscle (Fig. 3). There is sometimes an area of pigmentation about the opening, and occasionally a thickened bit of tissue may be felt which contains a bit of cartilage and is called the cervical auricle. The fistulous tract almost invariably runs upward and backward beneath the anterior portion of the sternomastoid muscle. It passes over the carotid sheath to the midportion of the posterior belly of the digastric muscle whence it arches medially behind the stylopharyngeus muscle to the tonsillar fossa. By tugging at the skin over the opening one can often feel the cord-like structure extending under the sternomastoid.

Bearing in mind the close relationship that exists between the anatomy and histology of branchial fistulas and the embryology of the thymic duct, one must readily agree with Wenglowski that the origin of this condition must be attributed to vestigial remains of the thymic duct. Contradicting this theory some authors argue, that one occasionally sees a fistulous opening in the region of the ear, which is above the level of the third pouch. These are probably either secondary to infection or in most cases are rudimentary external ear canals from the first groove.

With the typical clinical picture, a diagnosis is usually comparatively easy. As a further aid in diagnosis, Hamilton Bailey, in 1922, demonstrated the presence of cholesterol crystals on microscopic examination of aspirated content in some cases. Wangensteen gives a further aid to differential diagnosis by X-ray examination, suggesting aspiration through a needle and injection of a medium opaque to the X-ray (Fig. 4).

Differential diagnosis must be made from inflammatory and tuberculous adenitis, hygroma, thyroglossal duct, hæmangioma, and lipoma.

Inflammatory adenitis is often bilateral and numerous glands are involved. They are tender and the offending focus usually can be found in sore throats, tonsils, and teeth. Tuberculous glands may be more readily confused with cyst and fistula, but they are firm and tender, and other glands usually are involved and often matted together in a group. The discharge from the fistula in broken down glands is purulent while in branchial fistula it is clear mucoid or milky and may contain cholesterol crystals.

Fig. 4. Branchial fistula, lipiodol injection, showing characteristic extension beneath sternomastoid to middle portion of the posterior belly of the digastric muscle, where it arches medially to the tonsillar fossa.

Cystic hygroma is translucent, occurs most frequently in the supraclavicular area, is often lobulated, and may grow to enormous proportions extending up into the face in front of the ear.

The thyroglossal duct occurs invariably in the midline and moves up on swallowing.

Hæmangiomata decrease in size on pressure and have the typical discoloration.

Lipomata are lobulated, soft, and non-fluctuatory.

TREATMENT

Frequent incision and drainage is often the lot of these children before the condition is recognized and properly treated. Two of our 4 children had incision and drainage without benefit before entering hospital. Only complete surgical removal under general anæsthesia will effect a cure.

The extent of the sinus tract should be roughly determined before operation by injection of an opaque medium and X-ray (Fig. 4). Visualization of the tract may be facilitated by a simple method described by R. J. McNeill Love. A horse hair or dermal pursestring suture is placed about the fistulous opening and drawn taut to shut off secretion. In a few days the tract becomes distended and identification is then comparatively easy.

The injection of methyl blue as ordinarily carried out, is usually a messy job. As the tract is

Fig. 5. Excision of branchial fistula, showing armamentarium and method of massaging methyl blue into the tract.

Fig. 6. Excision of branchial fistula, showing a sistant's finger pushing outward in the region of the tonsillar fossa, as dissection is carried to the pharynx.

opened somewhere in the course of dissection, the dye spills, stains all the surrounding tissue, and all identification is lost. I have, however, found methyl blue to be a distinct aid when used in the following manner (Fig. 5):

The end of an ordinary hypodermic needle is broken and rounded off, the caliber of the needle depending upon the size of the fistulous opening. The direction of the tract is determined with a probe and the methyl blue then injected with the use of the blunted needle. Too great a pressure may rupture the tract and defeat the purpose of the injection. At the same time the fingers of the left hand gently massage the neck to and fro in the direction of the tract. Thus the epithelium in even the minutest diameter of the tubule may be reached and stained. Using the same syringe and needle we then gently but thoroughly wash out the methyl blue with water or saline, alternately massaging outwardly until the return is only faintly stained. In this manner the epithelial lining remains stained and if the tract is inadvertently opened during the dissection, no soiling of the neighboring structures will take place.

A small probe is again inserted and the incision made through skin and platysma along the anterior border of the sternomastoid and surrounding the fistulous opening. The platysma is reflected laterally on both sides, and the sinus is dissected to the pharynx in its entirety. The stump may be dealt with by several methods as recently described by Herbert Willy Meyer. By the method of von Hackerer a probe is passed through the lumen of the duct, into the pharynx, and with a suture the stump is attached to the probe and inverted into the mouth cavity and there tied and cut. By the method of Koenig a probe is forced into the pharynx a short distance from the duct which is then sutured and pulled with the probe into the pharynx, thus re-implanting it. The method of von Hackerer appears most desirable for several reasons; there is not the possibility of hæmorrhage from passage of the probe there is not the danger of opening of fresh avenue of infection from the mouth, and chiefly it does away with the entire tract. Minute tubules would, however, be rather difficult to invert.

I have found that dissection of the stump may be carried to the pharynx by simply having an assistant place a finger in the tonsillar fossa

Fig. 7, left. Thyroglossal cyst occurring at the level of the hyoid bone.

Fig. 8. Thyroglossal duct fistula, showing characteristic midline opening.

(Fig. 6). By having him push outward, the stump is cored out until it approaches the finger of the assistant when it is severed and touched with tincture of iodine. A small split tube is inserted for drainage for 24 hours and closure made in the usual manner.

THYROGLOSSAL DUCT

The development of thyroglossal duct cysts and fistulas is definitely established as being the result of a failure of the embryonic thryoglossal duct to become obliterated.

Clinical features. The condition is more common than branchial cysts and fistulas. At the Childrens Hospital there were 11 children who came to surgery for thyroglossal duct excision. Of these 6 were boys and 5 were girls. One was a negro boy, 2 were Mexican, 1 Italian, and the others of American families. The ages ranged from 2 to 11 years of age. In 1925, Klingenstein and Colp received 42 cases of thyroglossal ducts and in their series 31 were males and 11 females. Twenty-one occurred in the first decade, 10 in the second, 7 in the third, and so on. The oldest age at which the lesion was discovered was 35 years, the youngest, of course, at birth of which these were 5. In the Childrens Hospital series the onset at birth occurred in two instances. In the remainder, the age of onset was at 6 months, 18 months, 2, 3, 3, 6, 8, 9, and 11 years, respectively. Adequacy of drainage decides whether a cyst or fistula is formed. In the series of Colp and Klingenstein, there were 13 cysts, 20 fistulas, and a combination in 9 cases. In this series 3 were simple cysts, only 1 a simple sinus, and the remainder were fistulas which were associated with cystic formation.

The cyst may appear at any level from the foramen cæcum to the suprasternal notch, and the corresponding fistula may make its exit anywhere from the chin at the floor of the mouth to the suprasternal notch. It is rarely, however, that it appears above the hyoid. The majority of fistulas open below the hyoid and considerably higher than the suprasternal notch. All are invariably in the midline and may vary in size from a pea to a lemon (Fig. 7).

The clinical picture of the cyst is that of a painless, soft, fluctuatory, semifixed mass occurring in the midline of the neck and moving up on swallowing. With a fistulous opening there is either a continuous or intermittent drainage of a clear or milky solution (Fig. 8). Troublesome symptoms such as a choking sensation, difficulty in swallowing, and obstructive dyspnœa are rare, but secondary infection either ascending from the external opening or descending from the foramen cæcum, is fairly common. With infection, the process usually remains localized and discharges through the sinus opening, although occasionally a severe cellulitis of the neck develops. All too frequently the simple non-infected cyst is mistaken

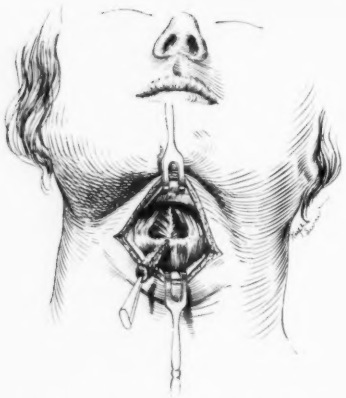

Fig. 9. Excision of thyroglossal duct fistula. The platysma muscle has been reflected and dissection carried to the hyoid bone.

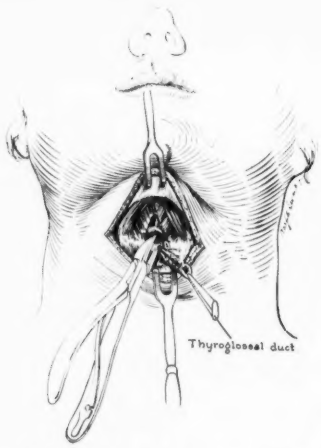

Fig. 10. Excision of thyroglossal duct fistula. The midportion of the hyoid bone is being removed with bone forceps according to the method of Sistrunk.

for an abscess, and consequently a history of repeated incision and drainage without cure is obtained. Two of our children had thus been treated, in one of which, a later attempt at removal had been undertaken, and in 2 other children, removal had been previously attempted but the operation had been without success in affecting a cure.

The sinus tract may pass over, through, or beneath the hyoid to the base of the tongue. The larger tract may be felt as a distinct tubule lying over the trachea and moving on swallowing. The lining consists of squamous epithelium surrounded by lymphoid tissue.

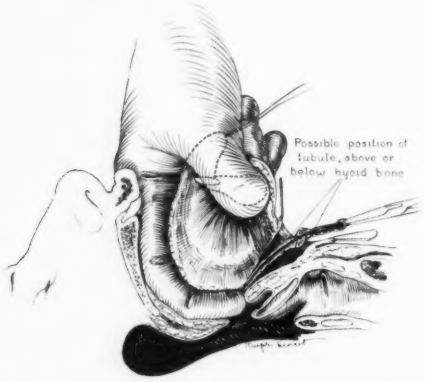

Fig. 11. Excision of thyroglossal duct fistula. The midportion of the hyoid bone has been removed. From this point the tract is cored out in the direction of the foramen cæcum, which is at about a 45 degree angle, with the patient in the goiter position. Dissection is carried up to a point where the finger at the foramen cæcum can be identified (Sistrunk).

Differential diagnosis must be made from ranula, adenitis, pyramidal lobe of the thyroid, and the branchial cleft anomalies.

Ranula of the sublingual gland occurs in the anterior part of the floor of the mouth and can be seen as a bluish cyst under the floor at the anterior part of the tongue and does not move on swallowing.

Adenitis, either single or tuberculous, occurring in the midline of the neck, is rare indeed, and is associated with other tender glands. Movement on swallowing does not take place.

A pyramidal lobe is attached to the thyroid near the isthmus. It is practically never enlarged unless it is associated with a goiter and it does not fluctuate.

TREATMENT

As in branchial cysts and fistulas, complete excision under general anæsthesia is the only cure. The fistulous tract should be stained according to the method described in treatment of branchial tracts.

W. E. Sistrunk has described a highly satisfactory method of removal and his is the technique I shall here describe.

A horizontal incision about 1½ inches long is made through skin and platysma and surrounding the sinus opening. The flaps are reflected and the dissection of the tract carried to the hyoid bone (Fig. 9). The sinus may pass over, through,

or beneath the hyoid bone to the foramen cæcum at the base of the tongue. Beyond the hyoid the tract frequently assumes minute proportions. To facilitate further removal, a section of the midportion of the hyoid is removed with bone cutting forceps (Fig. 10). An imaginary line is pictured from the hyoid to the middle of the base of the tongue. This is about at a 45 degree angle with the patient in a goiter position on the operating table. Dissection is carried further in the exact direction of the foramen cæcum. To orient himself and to aid the dissection, the surgeon places a second sterile glove and sleeve over the left hand. The index finger is placed in the mouth of the patient at the foramen cæcum and pushed out toward the hyoid bone. At the same time the fistulous tract is cored out to the base of the tongue (Fig. 11). A split tube drain is inserted, the cut ends of the hyoid approximated. The platysma is then sutured with interrupted plain No. 00 catgut and the skin closed in the usual manner.

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REACTIONS AFTER INTRAVENOUS INFUSIONS

A Further Report on Their Elimination[1]

LEE RADEMAKER, M.D., Philadelphia

In a previous report, the causative factors of reactions after intravenous infusions and the theoretical elimination of these reactions were discussed. Since that time Perkins has summarized the more recent literature and has discussed the subject in a very thorough way. It is the purpose of this contribution to discuss our practical experience in applying the principles developed in our previous report.

When beginning a study of intravenous solutions, an evident lack of organization and method of preparing solutions was evident in our hospital. Solutions were prepared in individual dressing rooms from bottles of commercial distilled water, many of which had been standing unused for months. Glassware was merely rinsed, and a commercial and impure glucose was used in the preparation of the solutions. The majority of glucose used came from ampuls of 50 per cent glucose from various manufacturers, being diluted with saline solution prepared in the hospital. Solutions of uncertain age were used, oftentimes a month old, due to the fact that flasks were labeled only on the initiative of the individual dressing room nurse. Needles were often rusty—tubing was prepared by boiling in a water sterilizer containing from 10 to 40 grains of bicarbonate in 3 gallons of water. From the standpoint of our later experiences it seems queer that an infusion could ever have been given under these circumstances without an accompanying reaction. Later a Barnstead single still was used, the water being distributed in bottles and again kept in dressing rooms for various intervals. This naturally gave no improvement.

When our new distillation apparatus was installed the first measure applied to correct all these evils was to install a central supply room, all solutions being prepared by one individual and delivered to wards and floors as requested. Later we found that even the shifting personnel of student nurses would not suffice because of interference with the work by other duties, and a graduate nurse was put in charge of all solutions. It is also advisable where possible to have all equipment for the administration of intravenous fluids taken care of in one central supply room, but this change we have not been able to effect here.

To apply the theories developed in our earlier work we applied first to the Barnstead Still and Sterilizer Company to design for us a suitable distillation apparatus. The still designed by them is of the continuous distillation type with horizontal condensor. Multiple baffle plates were placed in the upper portion of the still and a smaller set in the vertical portion of 3 inch pipe to the condensor. This system forces the steam to turn many angles, striking against numerous plates, thus losing its spray. In addition to this a deconcentrator tube as described by Severinghaus was attached. This consists of a ¼ inch brass pipe introduced through the bottom of the still and attached to the waste pipe by a valve and with an air vent. The tube rises vertically in the center of the reservoir about one-third of its height. The level of water is kept about one-half inch above the open end of the tube. When the valve is open the surface of the water is constantly in motion toward its center, which greatly diminishes the formation of spray. Increased concentration at the surface, which is another cause of spray formation, is also prevented by this tube. Other satisfactory distilling sets were on the market, especially the double and triple distillation outfits with baffle systems, and although these might be slightly more satisfactory, they were more expensive and did not promise to be much more effective in removing pyrogenic material. In the use of this apparatus we soon found it necessary to observe four rules:

1. To distill slowly: this prevents excessive foaming.
2. To distill for 15 minutes into waste: this acts to clean out accumulated products.
3. To deconcentrate with sufficient rapidity.
4. To clean entire apparatus regularly every 6 months, removing boiler scale and nitrogenous products.

Failure to observe any of these rules has resulted in reactions.

Since theoretically immediate sterilization should prevent formation of further pyrogen, the water was first distilled into a sterilizing tank equipped with cooling coils. As soon as sufficient amount of water was distilled it was sterilized and allowed to remain in the tank for 24 hours, except as used. We could demonstrate no

[1] From the Department of Surgery (Service B) University of Pennsylvania.

gross bacterial growth in this water, yet after a week of use reactions began to occur and we found the tank walls covered by a nitrogen containing material. Repeated cleansing failed to keep this tank clean and it was therefore abandoned. A 5 gallon glass tank was employed, but this developed the same difficulty, so that water has since been distilled into glass graduates and immediately made up into solution. We found that in a warm room a delay of sterilization of as little as 4 hours could generate enough pyrogenic material to produce reactions.

The source of contamination and the point of trouble can easily be located by applying the permanganate test described by Carter to water in each stage of production. The test as described can be further simplified by using 10 cubic centimeters of water for the test and titrating this against two hundredth normal potassium permanganate in a clean test tube, heating the water to boiling at intervals. If more than 1 cubic centimeter of permanganate is reduced the water is dangerous and if 5 cubic centimeters is reduced reactions are almost sure to occur. We have found this a very valuable test in locating the source of trouble when reactions occur. With the exception of a few instances when rules for distillation were badly disregarded, the distilled water has never reduced 1 cubic centimeter of the permanganate solution in this test. Obviously if the freshly distilled water is free of contaminant and reactions occur, contamination source must be at some place during preparation of solution and by testing each stage the source can be located.

The preparation of the solutions next received our attention. By using the test just described it was found that if glassware was merely rinsed or imperfectly washed pyrogen might accumulate in it by bacterial growth in small residues, even in the moisture lining flasks. Accordingly strict rules were developed for cleansing of all glassware. The flasks and graduates are first washed in tincture of green soap and hot water and rinsed in tap water. The standard cleaning solution of potassium bichromate and sulphuric acid is then used. The glassware is next rinsed four times with tap water and six times with freshly distilled water. It is then ready for use. If not used within 2 hours the entire procedure is repeated.

The chemical ingredient of each solution is added to the graduate of distilled water, stirred till dissolved, and the resulting solution is then filtered through a fine filter paper. Erlenmeyer flasks of a size twice the capacity of the solution contained are used to prevent splashing during autoclaving.

In previous times ampuls of 50 per cent glucose had been added to the salt solution or to distilled water to prepare the glucose solutions. This appeared to us unsatisfactory: fragments of glass from broken ampuls were constantly added to the intravenous solutions, with small amounts of alcohol used to sterilize the ampuls externally, and too, sterility seemed questionable. Moreover, each manufacturer claimed various advantages for his products and various staff members preferred different brands of glucose. Mallinckrodt's or Merck's anhydrous chemically pure glucose, bought in 100 pound lots and made up in our own solutions has proved very satisfactory and has reduced the cost of glucose solutions about 60 per cent. Glucose has been prepared in 5 and 10 per cent concentration. Sodium chloride is used in the usual tablets supplied by various manufacturers. The most used solution has been 5 per cent glucose in normal saline.

While seal with cork and paraffin seemed ideal from the point of view of permanency and completeness, objections were raised by members of the hospital staff who insisted that solutions should be no more than 24 hours old. For this reason the conventional seal of gauze, cotton, and waxed paper has been used. As the use of fresh solutions has necessitated a great deal of waste, we have been gradually increasing the length of time solutions may stand after sterilization without producing detrimental results, and we hope soon to apply the cork and paraffin seal so that we may keep the solutions 30 days. We find that the longer solutions can be kept the less is the waste and the greater is the economy in labor.

The speed of injections, temperature of solution, and amounts administered still persist in many minds as causative factors in producing unfavorable reactions.

Following the principles previously described, almost all of our solutions are given at room temperature. Continued venoclysis is given without heating save for running the tubing along the patient's arm. We have never seen untoward effects of too cold solutions. Speed of injection has no effect on producing pyrogenic reactions as far as we can determine, with the exception of the fact that fewer reactions occur with the use of venoclysis than in rapid intravenous injections. Pyrogenic reactions have, however, been observed repeatedly after hypodermoclysis, and certainly administration by this method is sufficiently slow.

The amount of solution administered may have a slight bearing. If 1,000 cubic centimeters of solution contains only sufficient pyrogen to cause

a reaction, one half that amount should not do so. On the other hand, with gross contamination, quantities as small as 50 to 100 cubic centimeters can give severe reactions.

In our previous work we were inclined to disbelieve any possible effect of rubber tubing in causing reactions despite the previous work of others. The grounds cited was the boiling of rubber with non-pyrogenic solutions and administration to dogs without reactions. This has been repeated recently with four varieties of new tubing, with the same result. Rubber tubing cannot be ruled out entirely on these grounds, however, since dogs are relatively insensible to reactions. One of our wards has been especially equipped with an intravenous tubing sold by Becton, Dickinson & Company. This tubing far excels ordinary tubing in durability, having withstood constant use for over 18 months without replacement. We have noted that although this ward used a great deal of intravenous fluid no reactions have occurred when this tubing was used. In many of the reactions recorded during the past year a history of new rubber tubing could be obtained. One particular instance presents some definite evidence that tubing may be an occasional causative factor.

A patient suffering from peritonitis after a ruptured appendix had received intravenous glucose and salt by venoclysis for 4 days without reaction. At this time the rubber tubing commenced to leak. The tubing was removed and a new set containing new rubber tubing was dropped into the same flask of solution previously in use and reconnected to the cannula in the vein. The patient received less than 100 cubic centimeters when a violent reaction occurred. Here all factors were unchanged except tubing.

Accordingly all our venoclysis sets and intravenous sets have been equipped with special Becton, Dickinson & Company tubing and this is further prepared by the Stokes technique, namely, filling the tubing with 10 per cent sodium hydroxide for 12 to 24 hours, washing in running water for 2 hours and boiling in distilled water for ½ hour before using. Since this was done we have had but 3 reactions from some three thousand liters of solution, 2 of which could be definitely traced to the necessity of cleaning the still, and all of which were mild. Rubber tubing offers another possible difficulty, however, in that it is frequently not sufficiently cleaned before using a second time, and contamination of the tubing occurs. This is especially true if a blood transfusion had been previously given. Scrupulous cleanliness and allowing waste of 100 cubic centimeters of solution through the needle before insertion into the vein are safeguards of this possibility.

RESULTS

Previous to the introduction of our new system, infusions were sparingly given, the clinician balancing always the beneficial effect against the dangers of reaction. The average consumption of intravenous solution was about 40 liters per month, and reactions occurred in 30 per cent of these. Since installation of the new system consumption has gradually raised until at present about 600 liters are used per month. Reactions have varied from 4 per cent to none in the various months as we encountered the difficulties described. During the past 2 months one mild reaction has occurred in 1,033 liters of solution used. During the last 3 months our central supply room has taken over the making up of sodium citrate solutions for transfusions, and even here we have noted a great decrease in the number of posttransfusion reactions of pyrogenic type.

The constant rise in consumption of solutions indicates to us an increasing confidence on the part of clinicians in the safety of solutions prepared. A very occasional and mild reaction still occurs, but because of the rarity of these reactions it is extremely difficult to determine their cause. Perhaps individual susceptibility is the final factor, over which we naturally have no control.

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POSTOPERATIVE SUPRAPUBIC FISTULA

Analysis of Causes

EDWIN BEER, M.D., F.A.C.S., New York

AMONG the annoying and tantalizing complications of suprapubic cystotomy, whether done for obstruction of the neck of the bladder or tumor of the bladder, is persistent fistulization or delayed healing of the suprapubic bladder incision. At times, such incisions fail to heal and there is continuous urinary leakage; in other cases the wound opens and closes with intermittent urinary leakage. Fortunately, after a careful study and recognition of the underlying cause, most of these patients can be definitely cured, and in our experience that has usually been the end-result. On the other hand, many patients have come to us in whom repeated attempts have been made to close the bladder fistula without satisfactory results.

During the last 20 odd years, it has been possible in studying these cases to arrive at a pretty definite understanding as to the underlying causes of delayed closure and repeated re-opening of the suprapubic wound. The causes of this trouble seem to be local in the majority of cases, but in other cases, the trouble appears to be due to disease in the proximal part of the urinary tract, while in others the urinary tract distal to the bladder is the essential factor.

Among the local causes of persistent fistula or recurring fistula of the bladder, the most common are connected with faulty technique of the operation, whether it be a one step or a two step prostatectomy, or a resection of the bladder for neoplasm. As a result either of poor operative technique or of the patient's vomiting and coughing after operation, the bladder wall may prolapse between the rectus muscles, with the result that a mucous membrane channel is formed which prevents the bladder from closing. In some cases, the mucous membrane channel even grows out through the muscles and unites with the skin, making a mucocutaneous fistula. It has been claimed by some that in opening the bladder, unless the incision is made high up near the dome, fistulization is liable to occur, but in our experience, irrespective of the site of incision, whether high or low, fistulization seems no more likely to occur with the low incision, than with the high incision in the bladder wall.

Foreign bodies left behind in the bladder, either stones or secondary growths, or even real foreign bodies, which become more or less encrusted with phosphatic material, are occasionally found to lead to protracted, slow closure of suprapubic wounds. Large diverticula of the bladder, which have been overlooked in the course of the operation on the bladder whether for stone or prostatic enlargement, especially if infected, are very liable to lead to slow healing of the suprapubic wound and often prevent definitive closure. After the diverticulum is removed, just as in the other group after the foreign body is removed, the suprapubic wound closes kindly, much to the surprise of every one concerned.

In addition to the conditions mentioned, small, contracted, fibrous bladders are very liable to lead to repeated fistulization of the cystotomy wound, and it is wise to avoid giving too good a prognosis in prostatic obstruction cases associated with contracted bladder, both as to the cure of the contracted bladder, and as to the relief of prostatic symptoms. Although one sees such cases completely relieved at times, in most instances the contracted bladder never dilates properly and as the patient's capacity remains small, the frequency persists, and, unfortunately, in these cases, fistulization is liable to be a disagreeable complication. In addition to this type of bladder, a cystostomy in the presence of urinary tuberculosis is practically always followed by fistulization, unless partial or complete exclusion of the tuberculous focus in the upper tract takes place.

Among the well recognized causes for fistulization of the bladder following cystotomy in the peripheral part of the urinary tract, are persistent obstruction at the neck of the bladder or in the urethra. Overlooked fibrous necks or overlooked prostatic adenoma masses are very liable to keep the suprapubic wound open, and naturally strictures in the urethra, stones in the urethra, or other disturbances in the peripheral urinary tract, predispose to this disagreeable complication. These causes are rather well recognized, and following transurethral section of the neck of the bladder with the electric cutting current, or dilatation of the stricture at the neck or in the urethra, or removal of the stones, the suprapubic fistula usually closes and stays closed permanently after a brief use of an indwelling urethral catheter. In some rare cases, neurogenic disturbances may

possibly underlie the delayed closure. In these disharmonies between the detrusor and sphincter muscles, the peripheral obstruction seems the important factor and it is relieved by use of an indwelling urethral catheter.

In the proximal part of the urinary tract, it is not generally appreciated that causes of continued and repeated opening of the bladder wound may be found. Infected calculous pyonephroses or infected hydronephroses, such as are occasionally seen after ureterovesical anastomoses, are not infrequent causes of persistent suprapubic fistula, and in our experience, after removal of such infected and infecting foci from the upper urinary tract, either by nephrectomy or by more conservative means, it is surprising to see how frequently the suprapubic fistula will close.

In this brief analysis of the various local, proximal, and peripheral causes of persistent suprapubic fistula, one must bear in mind that from the therapeutic standpoint our efforts must be of the simplest character while studying the case and deciding upon the cause of the trouble. Naturally, if indwelling catheter with cauterization of the sinus from without and cystoscopically, and occasional irrigations with silver nitrate solution of the bladder will lead to a closure of the fistula, it would be unwise to rush in and do a large secondary operation to remove a diverticulum or to remove a kidney, even if it be the site of calculous disease or be an infected hydronephrosis following some procedure on the ureter. If, however, local measures, such as have just been mentioned, fail to effect a definite closure of the suprapubic fistula, it may be necessary to do something more radical, which may consist of excision of the fistula and inversion of the bladder in mucocutaneous fistulæ, or excision of the diverticulum in cases associated with infected diverticulum. In other cases, section of the contracted fibrous neck, etc., and again, in other cases, the removal of the infected and infecting proximal segment, kidney and ureter, may be necessary before permanent closure of the fistula is obtained.

SUMMARY

Underlying causes of persistent and recurring suprapubic fistula following cystostomy.

A. Local.

1. Improper surgical technique and partial prolapse of the bladder wall between the rectus muscles.
2. Stones, gauze sponges left in bladder.
3. Contracted bladders.
4. Overlooked large, infected diverticula.
5. Disharmony between the sphincter and the detrusor muscles.

B. Peripheral.

1. Unrelieved obstruction at the neck of the bladder; fibrous necks, adenomata.
2. Strictures, stones, etc., in the urethra.

C. Central.

1. Infected stone kidneys, infected hydronephroses, and tuberculous kidneys.

CORRESPONDENCE

ETIOLOGY OF GASTRIC AND DUODENAL ULCER

To the Editor: I would like to add my own results[1,2] to the very interesting paper of Warren B. Matthews and Lester R. Dragstedt, in SURGERY, GYNECOLOGY AND OBSTETRICS, September 1932, p. 265.

Experimenting on dogs I found that ulcers in the duodenum (with the symptomatology of duodenal ulcer) could be produced in dogs simply by tying the main pancreatic duct. These ulcers were confirmed by microscopic and histological examination.

Melbourne, Australia. J. LEON JONA.

[1] JONA. M. J. Australia, March 2, 1918; April 19, 1919.
[2] Idem. An Experimental Study of Duodenal Ulcer. Melbourne, 1919.

JOHN B. MURPHY

Material is being collected for an authorized biography of Dr. John B. Murphy. If any reader of this JOURNAL has in his possession letters from Dr. Murphy, knowledge of facts concerning his life, or any other data, it would be appreciated if they were sent to the Editors. All material will be returned promptly and the source credited.

EDITORIALS

SURGERY, GYNECOLOGY AND OBSTETRICS

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DONALD C. BALFOUR, M.D.....Associate, Editorial Staff

MAY, 1933

CHRONIC ADHESIVE PERICARDITIS

FROM the standpoint of pathology there are three chief conceptions as to chronic adhesive pericarditis. In one there are adhesions between the heart and pericardium and also between the pericardium and surrounding structures, especially the chest wall —mediastinopericarditis. In the second, the pericarditis is a constricting one, and, in the third, the adhesions are found between the outer layer of the pericardium and surrounding structures, especially the pleura, without any involvement of the inner layer of the pericardial sac. This latter condition is common in fibroid phthisis with pleuritis, and in tuberculosis confined chiefly to one lung and pleura thus causing moderate displacement of the heart toward the affected side.

In pulmonary tuberculosis, the heart is usually small, either as a result of long rest, or because constricting pericarditis may be due to tuberculosis. This latter condition is rare, however.

The symptoms should make differentiation possible. In the external type of adhesive tuberculous pericarditis with or without displacement of the heart, even if the shadow is small, there should be no essential cardiac symptoms. In constricting pericarditis, the symptoms are striking: engorgement of the veins, chronic passive congestion, ascites, and anasarca, together with other symptoms characteristic of broken cardiac compensation. There is this difference however; the heart is not hypertrophied and dilated as it would be if valvular or myocardial disease were present.

There is a widespread belief that suppurative pericarditis, in those patients who survive operation, is apt to be followed by disabling pericardial adhesions. It is natural to assume that drainage of the pericardium is followed by adhesions between the parietal and visceral layers and the leaving of drainage material in the pericardial sac should increase this likelihood. The writer has operated on eleven patients with suppurative pericarditis, with six recoveries. The patients who recovered were children or young adults and all were followed for some time. One, the youngest, who was four years old at the time of operation, had a stormy early and late convalescence; for four months there were anasarca and ascites, and the peritoneal cavity was tapped several times. For the last several years he has grown normally however, and there has been no clinical evidence of cardiac disability. One patient, a nurse in training, for about a year after operation, was short of breath on unusual exertion. She was without other signs, however, and is now without symptoms. Another, a six year old child, developed a secondary walling off in the pericardial sac, high up and posterior, against

the left auricle, which required a second operation. This pocket was located with the X-ray and the examining finger, introduced along the drain tract in the pericardium, encountered fresh adhesions everywhere, and was thrust through the wall of solid exudate into the pocket of pus. In spite of this, the child, after a slow convalescence, was apparently well in six months and has since grown and behaved in a normal way. Two other patients were young adults and made good recoveries after a period of serious illness immediately following pericardiotomy. The last patient was operated on by a modified approach described elsewhere and made a more rapid recovery than any of the others. It was believed that better drainage was an important factor. He has been seen repeatedly and is not disabled.

One would expect to find, after such operations, extensive adhesions between the outer layer of the pericardium and the chest wall and pleura, where these structures form the boundaries of the "triangle of safety," especially if no attempt is made to fasten the edges of the incised pericardium to the subcutaneous tissues. If such adhesions do occur, the pathological findings should closely resemble the condition found in the mediastinopericarditis, and the disability resulting would call for the procedure of Brauer.

The pericardium follows the heart closely in its movements. It is easy to understand therefore that, if non-constricting adhesions occur between the two layers of the pericardium, no very great handicap may be imposed upon the heart action unless the outer layer of the pericardium is adherent to the surrounding structures, and, even then, limitation of motion may not be marked unless the surrounding structures are unyielding. It is upon this assumption that the whole procedure of Brauer is based.

In my own experiences I have been surprised that pus escaping from the incision in the pericardium has not percolated into the middle mediastinum between the two pleuræ and the pericardium, or even into the posterior mediastinum, as the potential space between the two edges of the pleura just behind the sternum and in front of the pericardium (the "triangle of safety") is continuous with the middle and posterior mediastinum unless shut off by adhesions between the pericardium and pleura. There has been very little evidence that such an extension of infection has occurred, and no patient has, as yet, presented any of the symptoms and signs associated with chronic adhesive mediastinopericarditis. I am quite sure that the outer layer of the pericardium does become to some extent adherent to the structures surrounding it, but I have not observed any evidence that there are adhesions between the pericardium and the unyielding bony and cartilaginous chest wall. It is certain that some individuals with rheumatic pericarditis develop widespread and dense adhesions between the heart and pericardium; between the pericardium and surrounding soft parts; and between these structures and the chest wall. Pericardiotomy with an open and discharging drain tract is bound to be followed by extensive infection. Just why dense and widespread adhesions are apparently not present as a postoperative complication is not at all clear.

One factor, however, may explain much. The patients who recovered had suppurative pericarditis uncomplicated by empyema and, in most instances, the infecting organism was the pneumococcus. In the peritoneum and in the meninges, the pneumococcus causes a very fatal infection, but, in the pleura and in the pericardium, this infection is relatively less destructive of life. ARTHUR M. SHIPLEY.

THE CHANGING TREND IN SURGICAL TECHNIQUE

IT is almost impossible for the busy worker in his generation to evaluate the changes that are constantly unfolding themselves before his vision. The more diversified these changes become, the greater is the difficulty of correct appraisal. It seems justifiable to remark that at no other time have changes in the social, economic, and scientific aspects of modern civilization progressed more rapidly than now. The practice of surgery shares equally in these changes. To many caught in the hurly-burly of active life it is impossible, and probably seems unnecessary, to stop and scan the progress that is being made, though it undoubtedly is wise to check up from time to time on the direction toward which general advances are being made and to emphasize the tendencies which seem to offer the greater progress.

Occasionally, philosophical contributions to our surgical literature appear in which the author is courageous enough even to contemplate the future, such as the delightful essay entitled "La Chirurgie de la Douleur" by René Leriche. Such a contribution must have for its inception a complete understanding of the actual state of practice in our time and represents a thoughtful attitude that in the long run is sure to exert a beneficial influence upon our field of work.

Recently driven by an interest in the surgical literature of that great epoch between the advent of anæsthesia and the discovery of bacteriology, I found myself plunged into that era of surgery in which great speed in operating was a dominant characteristic. This led to what I have chosen to call "ablation" surgery. Great portions of the body were removed rapidly with the knife in order to get rid of a small diseased part. This speed was partly a legacy from the time when anæsthesia was unknown and when speed in operating therefore diminished suffering. But it was also dictated by the fear of what might happen were the patient kept too long asleep, a fear engendered by the spectre of "ether pneumonia"! Lastly, the speed represented the lack of a philosophical attitude toward the advent of anæsthesia, without doubt one of the greatest gifts our profession has ever made toward the comfort of man.

One of the chief tendencies in our modern development is the abolition of this attitude toward surgery. The enormous experience with modern anæsthetics has given us great confidence in their safety and, in particular, the amount and duration of the anæsthesia has been shown to play but a minor rôle in postoperative complications. Speed, once a necessity and therefore fashionable and popular, has been shown to be not only a non-essential but a positive menace. Surgery, now rid of the specter of speed as a necessity, has learned, in this country largely through the influence of Halsted and his pupils, a new, meticulous and gentle technique which considers every cell as valuable unless diseased.

To be sure, amputations are still necessary, but they are performed in modern clinics only after every effort has been made to save the limb as a whole. This change of attitude toward the removal of major parts of the body is emphasized in the very critical studies relating to the possibility of restoring to a limb in which there is a damaged circulation sufficient blood supply to maintain the limb in a useful condition. The whole matter of sympathectomy in relation to impeded vascular channels and the great development of methods for testing the circulation of a limb and its possible restoration is an example of this. Technical improvements not only have permitted us this philosophical change toward

disease in surgical conditions but have enabled us to attack conditions heretofore too dangerous for operative intervention. Thus, the introduction of electrosurgery has enabled surgeons to attempt the removal of tumors such as those in the brain, heretofore forbidden them. Whether the removal of such diseased parts is worth the price in suffering and economic loss, end-result studies of survivals alone will tell.

This tendency for the preservation of all structures not actually diseased is constantly brought before us in the ever increasing and intelligent use of radiation in relation to tumors. Experienced surgeons fully appreciate the futility of surgical procedures in relation to certain very malignant tumors. Increasing diagnostic ability, in which the X-ray has proved of great assistance, has led to the early recognition of distant metastases, thus helping the surgeon to withhold a mutilating and useless procedure. Moreover, we are now learning the great possibilities of radiation as a means of therapy in the treatment of neoplasms. So much have we learned of this that it may be said the day is almost at hand when the scalpel will not be considered in the treatment of certain of the more malignant sarcomata and embryonic forms of neoplastic growth.

Still more recently it has been shown that the eradication of certain congenital sinuses and fistulous tracts by a caustic solution may be a better method than the excision of these tracts with the scalpel. None of the methods are really new, since the use of caustics and the cautery were methods practiced by Hippocrates and held equal position with the scalpel in the field of surgical therapy.

It appears that surgery today is characterized by a very sincere appreciation on the part of surgeons that every bit of tissue possible should be saved and particularly that structures taking part in important functions must be preserved. To this end we find introduced a great variety of new technical methods which seem increasingly to represent the one thing that has characterized the practice of medicine and surgery from a distant past, that is, to give to each individual patient the maximum benefit which can be given. It is perhaps surprising, though surely worthy of our great tradition, that in a day when scientific attitudes hold such a distinguished position in both the professional and public eye the profession of medicine, in spite of its tremendous interest in the progress of science and its understanding of disease, can still treat the patient rather than the disease.

ELLIOTT C. CUTLER.

EARLY AMERICAN MEDICAL SCHOOLS

THE COLLEGE OF PHYSICIANS AND SURGEONS OF CHICAGO

CHARLES DAVISON, A.M., M.D., F.A.C.S., CHICAGO
Professor of Surgery, Emeritus, University of Illinois

THE College of Physicians and Surgeons of Chicago was incorporated October 14, 1881. It was located at the corner of Harrison and Honore Streets, directly opposite the entrance to Cook County Hospital.

The College of Physicians and Surgeons was founded at a time when medical schools were largely proprietory institutions, owned and conducted by medical men. The founders were a group of young, active, pushing, ambitious medical men, experienced as junior members of the faculties of the existing medical colleges of Chicago. They sensed the timely opportunity for the entrance into Chicago of a new medical college. They appreciated the pedigogical value of graded courses of instruction. They recognized the proximity to Cook County Hospital as a great clinical teaching opportunity. They foresaw prestige and professional advancement for the members of the faculty of a new successful institution. They hoped for a profitable enterprise.

The original capital stock of the corporation was thirty thousand dollars, which was subscribed equally by the incorporators. Upon organization of the original faculty, the capital stock was increased to sixty thousand dollars, each additional member of the faculty being allotted stock to the amount of two thousand dollars.

The founders of the College of Physicians and Surgeons were A. Reeves Jackson, president, professor of surgical diseases of women and clinical gynecology; Samuel A. McWilliams, vice-president, professor of clinical medicine, diseases of the chest and physical diagnosis; Daniel A. K. Steele, secretary, professor of orthopedic surgery; Leonard St. John, treasurer, professor of demonstrations of surgery, surgical appliances and minor surgery; and Charles Warrington Earle, professor of obstetrics. During the organization period there were added to the faculty, among others, such well known men as Robert L. Rea, professor of principles and practice of surgery and clinical surgery; Frank E. Waxham, professor of diseases of children; Henry Palmer, professor of operative surgery, clinical surgery, and surgical pathology; John E. Harper, professor of ophthalmology; Oscar A. King, professor of diseases of the mind and nervous system; Henry Parker Newman, lecturer on obstetrics; Boerne Bettman, lecturer on ophthalmology and otology; G. Frank Lydston, lecturer on genito-urinary diseases.

The formal opening of the new institution occurred September 26, 1882, with 100 matriculated students present. The number of students in attendance gradually increased to 165, of which 52 graduated at the end of the session.

The clinical instruction to this class of students was given in the college amphitheater, the West Side Dispensary in the college building, the Illinois Charitable Eye and Ear Infirmary, and Cook County Hospital.

During the period of organization it was planned to present the entire subject of medicine in three annual pedigogically graded courses. The first year was planned to cover the fundamental subjects of anatomy, physiology, histology, chemistry, materia medica, therapeutics, and individual laboratory work; the second year to cover the principles of medicine, surgery, obstetrics, and the specialties; and the third year the practice of medicine, surgery, obstetrics, and their specialties, especially stressing a practical clinical training.

William E. Quine was appointed professor of medicine at the beginning of the second year, and thereafter the affairs of the institution were marked by his earnest, forceful, dominant personality. Nicholas Senn was appointed professor of surgery in 1882 and continued for 6 years with the institution. Christian Fenger, the great clinical pathologist and surgeon, was appointed professor of surgery at the beginning of the third year and occupied that chair for 9 years.

During the first 10 years the trials and difficulties of the college as a private institution were great. The administration of the institution was attended by ceaseless turmoil. There were fre-

quent changes in the faculty, accompanied by great dissatisfaction, largely due to the policy which limited the faculty positions to those who owned the stock originally covering that particular subject. Charles Warrington Earle, who was one of the most stormy, most persistent, and most capable of the objectors to the policies of the administration, was ousted. The college was not self supporting. The deficit at the end of 10 years was thirty thousand dollars.

At this crisis, in 1892, Dr. Quine with the collaboration of Drs. Steele and Jackson, managed a reorganization. Charles Warrington Earle was made vice-president and professor of obstetrics, and Dr. Quine president of the faculty. During this period there were notable additions to the faculty: John B. Murphy in clinical surgery, Henry T. Byford in gynecology, William A. Pusey in dermatology, Walter S. Christopher in pediatrics, Ludvig Hektoen and later William A. Evans in pathology.

A laboratory building with complete accommodations for the departments of anatomy, histology, embryology, biology, chemistry, and pathology was erected and occupied in 1893.

The Quine Library, founded at this time, became the depository of many medical books presented by Dr. Quine and other members of the faculty and their friends.

The West Side Hospital was organized in 1896 by medical practitioners interested in the college, and soon became a center of college clinical activity.

These were years of material prosperity for the college; there were more than 300 students in attendance in 1896. William A. Pusey was secretary. His vigorous activities added greatly to the prestige of the institution.

A new era in medical education was developing. The day of private medical schools was passing. The university plan of medical education was in evidence. The American Medical Association was demanding preliminary university training as an essential premedical requisite. There was a general effort being made throughout the country to bring the well established independent medical schools into organic relationship with the universities. The Chicago Medical College, one of the earliest and best medical institutions in Chicago, had been incorporated in Northwestern University as its medical department. Rush Medical College had affiliated with the University of Chicago.

Under these circumstances it was very reasonable that the University of Illinois should desire an affiliation with the strongest independent medical institution in the state; it was very reasonable that the College of Physicians and Surgeons would welcome the prestige of a connection with the state university.

Acting upon a suggestion of Governor Altgeld to Dr. Quine and to the board of trustees of the university an affiliation agreement between these institutions was signed April 1, 1897. By its terms the College of Physicians and Surgeons was leased to the University of Illinois as its medical department for the period of 4 years. The medical college was conducted by the same individuals as officers and faculty, but under the technical supervision of the University of Illinois. The university assumed no financial responsibility.

The results of this experiment were so satisfactory that an extension agreement was made for 25 years, beginning May 1, 1900, at the termination of which ownership of the College and all of its property was to be vested in the university. During this period one-third of the net profits was to go to the university and two-thirds to the stockholders of the college corporation. The institution was designated as the "College of Physicians and Surgeons, College of Medicine of the University of Illinois." This arrangement was followed by an era of prosperity with a rapid increase in student attendance, reaching at one time a registration of 710.

Accommodations in the original building having become inadequate, by agreement with the trustees of the university the adjoining public school property was purchased in 1900 by the college corporation and converted into a medical college building, thus greatly increasing the debt of the corporation.

The University Hospital was built and equipped by a small group of the faculty to provide more stable clinical teaching facilities.

The more rigorous requirements in medical education, the insistent demands for more adequate equipment and more elaborate methods of teaching increased the cost of administration. The requirements of higher standards of admission diminished the number of students and therefore the income. The financial condition of the college became almost untenable. To avoid the criticism that any appropriation by the legislature might directly or indirectly aid a private corporation, the 25 year partnership agreement was abrogated and a direct lease to the university of the college property for eighteen thousand, five hundred dollars a year was substituted.

Efforts by the university to obtain financial aid for the medical department from the legisla-

The College of Physicians and Surgeons of Chicago.

ture failed on several occasions because of legislative technicalities and antagonistic litigation. No part of the general appropriation of the university could be used legally for the support of the medical school; the income of the medical school was derived entirely from student fees. The trustees had never expended a single dollar of money appropriated by the state to the university upon the medical department.

The existing conditions were so unsatisfactory to the directors of the College of Physicians and Surgeons that they decided to continue no longer the lease of their property to the university. Accordingly, President James discontinued the medical department of the university on April 30, 1912.

The announcement by Dean Quine that the medical school would no longer be leased to the University of Illinois and that the College of Physicians and Surgeons of Chicago would reopen its medical school caused great consternation among the faculty, students, and medical alumni. An active and influential group of the faculty refused to take part in the reorganization of the College of Physicians and Surgeons as a teaching body. These men hoped for the continuance of a medical school in Chicago under control of the University of Illinois. The annual election of the medical alumni resulted in an overwhelming victory in the interests of the university.

About this time it was suggested by President James that if it were possible for the medical alumni to gather up the stock of the corporation of the College of Physicians and Surgeons and present it outright to the University of Illinois together with the absolute ownership and control of the property, it would be the best solution of the difficult problem; it would save to the university the fruits of its previous work in medical education; it would prevent the rivalry incident to another medical college being introduced into the field; it would bring back into the fold the friends of the College of Physicians and Surgeons, and it would furnish a plant already in existence under the absolute control of the university in which to conduct its medical work.

The alumni association recognized that to obtain all of this stock by donation or purchase in a limited time would require an unanimity of effort between the alumni, active friends of the university, and influential representatives of the College of Physicians and Surgeons. With this in view, a committee was appointed by the alumni association to take charge of the efforts to secure the stock for the university. This committee consisted of Edward Louis Heintz, president of the Medical Alumni Association, D. A. K. Steele, president of the College of Physicians and Surgeons, and the writer, an ex-trustee of the University of Illinois.

After an intense campaign by this committee, possession of the entire issue of stock of the College of Physicians and Surgeons was secured by donation, subscription, and purchase, for a gift to the university. The complete stock issue of 2,170 shares of the Corporation of the College of Physicians and Surgeons of Chicago; deeds to its real estate subject to certain encumbrances; a bill of sale of its personal property; its scholarship investments; its balance in bank ($12,551.11); and the resignations of the officers of the corporation were delivered to the president of the board of trustees by this committee as a gift to the University of Illinois from the Medical Alumni Association of the University of Illinois.

The board of trustees formally accepted the gift on behalf of the University of Illinois on February 12, 1913, and directed the president of the university to reopen immediately the medical department.

The College of Physicians and Surgeons of Chicago passed out of existence when this transfer was completed. It has become a memory—a pleasant memory to some of the older members of its faculty, increasingly pleasant with the reverie of the years.

THE SURGEON'S LIBRARY

REVIEWS OF NEW BOOKS

CHRISTOPHER'S *Minor Surgery*,[1] now in its second edition, promises to become one of the standard American textbooks on the subject. The thoroughness with which Dr. Christopher has covered the literature is evidenced on every page and it is a pleasure to see that procedures and ideas emanating from other sources are duly credited, even though the author may not at times agree. Although numerous methods of treatment are frequently outlined for a single condition, Christopher indicates his choice and the logic upon which the choice has been made.

The book is profusely illustrated with numerous line drawings and photographs of diseased conditions and procedures. It would be very difficult to duplicate these illustrations without consulting many textbooks. The value of the book to the young practitioner and the interne is considerable, since in it are described all of the minor surgical procedures and technical procedures which they are called upon to perform. Since the book is restricted to minor surgery, it deals often with subjects which are but cursorily treated in textbooks of surgery. Genito-urinary, orthopedic, gynecologic, and rectal conditions, so long as they belong properly to the realm of minor surgery, are fully described, thus making reference to special textbooks unnecessary. A broad conception of surgery such as Christopher has shown is both welcome and refreshing.

MICHAEL L. MASON.

THE outstanding contributions to large bowel surgery by the Mayos, Judd, and Rankin are epitomized in Rankin's recent book.[2] It will, therefore, be widely read and constitutes a valuable reference book on this subject. Emphasis is placed on the importance of malignancy, contributing two-thirds of the major lesions of the large bowel and rectum. Accepted methods of diagnosis and treatment are considered. In particular, consideration is given to the roentgenoscopic examination of the large bowel which "now permits accurate localization and recognition of the pathologic type in more than 95 per cent of lesions of the large bowel." Statistical data dealing with operability, operative mortality, and longevity, following surgical procedures in malignancy, offer encouragement to patients so afflicted and reflect the advances made in the surgical management of these diseases.

The chapters on anatomy, physiology, and congenital malformation of the rectum are excellent, both from the standpoint of text and illustrations.

The chapter on diverticulosis and diverticulitis is based on the study of a large number of patients and summarizes the many contributions to the subject of the Mayo group. The drawings illustrating the early beginnings of diverticula of the colon substantiate the Beer theory of origin; namely, that herniations of mucosa occur through weakened or fragmented circular muscle fibers of the large bowel.

In the treatment of megacolon the classical contributions of Judd and Adson and Rankin and Learmonth on lumbar sympathetic ganglionectomy are given careful description and illustration.

A detailed account is given of the bacteriological causes and experimental production of ulcerative colitis, based on Bargen's work. While many workers in this field may not agree with the importance of the diplo-streptococci as a causative factor, the evidence is fairly presented and therefore must stand the test of time and further study. The description and illustrations of the proctoscopic examination of the bowel with the varying changes in the mucosa in different stages of the disease are of great importance to the diagnostician. The entire chapter is one to be highly recommended to all those who have suffered with their patients in the treatment of this disease.

The chapter of polyposis considers thoroughly the pathology and tendency to malignant degeneration of polyps which stud the whole colon from the cæcum to the anus, in the condition known as multiple polyposis. To the casual reader it may not be apparent that the pedunculated adenomata described under the heading of "benign and rare tumors" are by far the most common type of mucosal polyps found in the rectum and colon. These are often present in young childhood, and in the opinion of the reviewer, are by gross and microscopic examination and course, nearly always benign.

The material presented on cancer of the colon and rectum is splendid. It reflects the outstanding work in this field at the Mayo Clinic and presents a chapter of exceeding interest to all who are concerned in the surgery of cancer. If for no other reason, these chapters fully justify the book. One of the outstanding contributions to colon surgery is Rankin's modification of the Mikulicz operation which he calls obstructive resection. A review of the rather dis-

[1] MINOR SURGERY. By Frederick Christopher, S.B., M.D., F.A.C.S. With a foreword by Allen B. Kanavel, M.D., F.A.C.S. 2d ed. Philadelphia and London: W. B. Saunders Company, 1932.

[2] THE COLON, RECTUM, AND ANUS. By Fred W. Rankin, B.A., M.A., M.D., F.A.C.S., J. Arnold Bargen, B.S., M.D., M.S. (Med.), F.A.C.P., Louis A. Buie, B.A., M.D., F.A.C.S. Philadelphia and London: W. B. Saunders Co., 1932.

couraging results of cancer of the rectum by radium treatment is given by Bowing.

In discussing the causes of rectal stricture the authors properly throw doubt on the importance of tertiary syphilis as a causative factor. Lymphogranuloma inguinale and its identifying Frei test is not mentioned as a possible cause of rectal stricture, but it is of course true that this factor is not definitely established.

In the chapters given over to anal infections, pruritis ani, and hæmorrhoids, there are numerous points where honest difference of opinion exists. For example, the author's statement that "the supposed incomplete external fistula is an impossibility," lacks authority.

The concluding chapter on operative procedures is well done and includes, as do most chapters in the book, a good bibliography. VERNON DAVID.

THE authors of *Treatment of Syphilis*[1] have endeavored to present this important subject in as condensed and simple form as is possible. In this they have succeeded well. There are thirty-three chapters, eleven of which are devoted to the various methods of administering mercury in syphilis, the pharmacology and chemotherapy of mercury, and the histological changes induced by it, and mercurial reactions, and their treatment. Two large chapters are devoted to bismuth therapy.

There are twelve chapters in which the arsenobenzenes are discussed. This discussion includes the history of their development, their chemotherapy, and toxicity, and the methods of their distribution and excretion. Reactions and fatalities following their use are thoroughly treated, and the technique of their administration is described in detail.

Two chapters are taken up with a discussion of the iodides and other metals, and one chapter is given over to the prophylaxis of syphilis.

The book is a fairly large one, and the subject is covered most thoroughly. The text is replete with references to the current literature, both foreign and domestic. The bibliography is indexed in an orderly manner and is a complete one. There are 62 excellent illustrations.

For anyone interested in the subject of syphilis, whether he be general practitioner or specialist, this book should prove to be of inestimable value. It is an excellent treatise and a distinct contribution to the subject of syphilis. EDWARD A. OLIVER.

IN his monograph[2] Rydberg has presented a very complete study of cerebral injury in newborn children from both the clinical and the pathological anatomical aspects. He lays a logical foundation for his study in a review of the normal anatomy and histology of the cerebral structures. This portion of the work receives wider treatment than the main subject would seem to warrant. The author, from his investigations, agrees with the present accepted theories regarding the origin and development of the glial structures except in the case of the amœboid microglia. His observations on human and animal fetal brains reveal all evidences to be in favor of the common ectodermal origin of the whole glia.

He discusses at length theories dealing with the pathogenesis of intracranial bleedings in the newborn, and records theoretical and experimental observations as to the influence of the birth process upon the blood circulation in the fetus.

The author also records the anatomical observations on a series of autopsies upon 100 consecutive newborn fetuses dying during partus or within 10 days thereafter. He made a very complete gross and microscopic study of these specimens and has correlated them carefully with the clinical manifestations. The symptomatology and diagnosis of birth trauma brain injuries is thoroughly covered and chapters are devoted to prognosis and treatment of these conditions.

The case records of 50 cases observed by the author form an appendix of value to the obstetrician, the pediatrician, and the neurologist. The work is complete with a large and inclusive bibliography. HALE HAVEN.

THE new *Textbook of Pathology*[3] by Boyd is admittedly not intended for practitioners of medicine or of pathology, but for students of pathology only. The practitioner, says Dr. Boyd in his preface, needs a book of reference. The student, on the other hand, needs a book from which he can "gain a grasp of the fundamental principles underlying the subject." His time is too limited to permit its dissipation in "intriguing rareties or the newest notion of the moment." With this audience and these ideals in view Dr. Boyd has produced a textbook of pathology which is smaller by almost a hundred pages of text than any of the three best known textbooks on this subject now in use in America. The preface is not the least interesting part of the volume inasmuch as it gives a clear statement concerning the changed outlook of pathology and its relation to other branches of medical science.

In accordance with the usual custom in books on this subject, this volume is divided into two parts. Part I deals with general pathology, which is "the elucidation of the vital processes which underly the end-results studied by the morbid anatomist . . . the study of disease from the physiological point of view." The book opens with a chapter on inflammation, which "forms the best starting point for the study of pathology as a whole." Without making inflammation a purposive reaction, the discussion emphasizes the functional side of all phases of the

[1] TREATMENT OF SYPHILIS. By Jay F. Schamberg, A.B., M.D., and Carroll S. Wright, B.S., M.D. New York and London: D. Appleton and Company, 1932.

[2] CEREBRAL INJURY IN NEW-BORN CHILDREN CONSEQUENT ON BIRTH TRAUMA; WITH AN INQUIRY INTO THE NORMAL AND PATHOLOGICAL ANATOMY OF THE NEUROGLIA. By Erik Rydberg. Copenhagen: Levin & Munksgaard, 1932.

[3] A TEXTBOOK OF PATHOLOGY; AN INTRODUCTION TO THE STUDY OF MEDICINE. By William Boyd, M.D., M.R.C.P. (Ed.), F.R.C.P. (Lond.), Dipl. Psych., F.R.C.S. Philadelphia: Lea and Febiger, 1932.

process. The chapters on infection and immunity, degenerative processes, circulatory disturbances, animal parasites, infectious granulomata present clearly the important established facts concerning these subjects. The chapter on tumors is limited to 54 pages and is perhaps too brief, especially the discussion of some types of tumors, to give the student an adequate comprehension of the subject.

Part II, special pathology, begins with a discussion of the pathology of the heart and blood vessels and proceeds through the various organs and systems of organs. The section on nephritis is especially to be commended for both its brevity and its comprehensiveness. A helpful discussion of the newer established facts concerning the physiology of the female generative organs, of bone, and of the glands of internal secretion opens the chapters dealing with the pathology of these organs. Throughout the volume paragraphs on "relation of symptoms to lesions" should stimulate in the student an interest in the subject.

The literary style of the author is clear, concise, stimulating, and interspersed with numerous striking bits of description and allusions that make the reading of this volume a pleasure. He speaks of cells "trapped in the pathless forest of the pulp" of the spleen. In connection with syphilis of bone he refers to "the nocturnal boring pains alluded to by the Psalmist." The incidental historical reference to the discovery of tar cancer on page 229 is especially interesting and should give to students a correct viewpoint toward research. The otherwise delightful literary style is marred by only one fault, namely, the use of too many short sentences.

The volume can be commended for its clearness, its conciseness, and its readability. It will, on most subjects, meet adequately the needs of medical students. It may also be read with profit by practitioners of medicine and surgery who desire "to indulge in the periodic brain-dusting recommended by Osler," and to acquaint themselves with the modern point of view of pathology which is no longer "an outworn creed, a science as dead as the material with which it deals." "Pathology in relation to the living patient is the motif of this book." The subtitle, "An Introduction to Medicine," is therefore justified.

J. P. SIMONDS.

IN a 325 page monograph[1] Grollman discusses the subject of the amount of blood pumped by the heart in unit time. Dr. Grollman is associate professor of physiology in the Medical School of Johns Hopkins University and has devoted a number of years to this type of study. The book contains a critical review of the various methods formerly in use and a detailed account of the acetylene method.

The physiological variations of the cardiac type as studied by this method include the effects of posture, ingestion of food and fluids, sleep, menstruation, emotion, temperament, exercise, and altitude. Another series of studies were made of the changes of cardiac output considering the effects of alcohol, caffeine, tobacco, carbon-dioxide, adrenalin, and the vaso-depressants. The cardiac output was studied in various types of cardiovascular diseases and abnormal cardiac physiology.

The bibliography is complete and the book is well indexed. The printing and binding are excellent. It will be of particular interest to those who are active in research in cardiovascular physiology in the clinic or in the laboratory. CHAUNCEY C. MAHER.

ENDOCRINE medicine is discussed by Engelbach[2] in a 3 volume work of over 1800 pages profusely illustrated. The first volume, on general considerations, covers the research history, anatomical development, physiology of the endocrine glands; the etiology of their diseases; diagnostic procedure; and the relation of endocrine disorders to public health. The second and third volumes are composed of four main sections in which endocrine diseases of infancy, juvenility, adolescence, and maturity are discussed. The emphasis throughout the work, therefore, is on the life-long character of the endocrinopathies and on their appearance in all age periods. This point of view is in some part due to the demonstration of the growth hormone. Abnormality of this function of the anterior pituitary must be determined by comparison with a normal curve of growth. A valuable feature of this work is the inclusion of tables of measurements and X-ray studies of bones from infancy to maturity. The prominence given the infantile and juvenile endocrinopathies is justified by statistical analysis of the 2,000 cases which make up the clinical basis of the book. Of the diseases occurring in this series, 40 per cent were believed to have started in infancy or childhood. It is axiomatic in general medicine that prevention is the best treatment; obviously in this group of diseases prevention of adult disorder begins during embryonic life; hence, the endocrine status of the mother must be analyzed and corrected. To follow out the same line of thought, a section on senility should be added.

The adult endocrinopathies covered in section five are thyroid disorders, hypophyseal disorders, composed of anterior lobe pituitarisms, adiposogenital pituitarism, pituitary tumors, and neuro-pituitary disorders, bi-glandular disorders of the thyroid and pituitary, gonadal disease, and thymic syndromata. Parathyroid conditions, covered originally as they appear in infancy and childhood, are again described in a single chapter relating to adolescence and maturity. In this discussion tetany and hyperparathyroidism are presented.

[1] THE CARDIAC OUTPUT OF MAN IN HEALTH AND DISEASE. By Arthur Grollman, Ph.D., M.D. Springfield, Illinois, and Baltimore, Maryland: Charles C. Thomas, 1932.

[2] ENDOCRINE MEDICINE. By William Engelbach, M.D., F.A.C.P., B.S., M.S., D.Sc. With a foreword by Lewellys F. Barker. Vol. i.—General Considerations; Vol. ii.—The Infantile Endocrinopathies. The Juvenile Endocrinopathies; Vol. iii.—The Adolescent Endocrinopathies. The Adult Endocrinopathies. Springfield, Illinois, and Baltimore, Maryland: Charles C. Thomas, 1932.

Throughout all sections case histories are used, charts given, X-rays and histological sections reproduced, and therapeutic experience quoted. The hormone preparations now available are evaluated and indications for their use given.

The complete picture of endocrine physiology and disease in man will not be presented for many years. At the present time this work describes well known endocrine entities in the light of the latest discoveries but, in addition, will have a permanent place in medical literature because of its teaching of the endocrinopathies as life-long processes beginning in infancy and continuing on through childhood, adolescence, and maturity.

A fourth volume is being prepared for the diseases of the pancreas, suprarenals, and liver.

PAUL STARR.

AZEMA presents a comprehensive monograph[1] on spondylolisthesis. After a short historical review, he enters into an extensive discussion of the lumbosacral anatomy and the mechanics resulting in the anterior displacement of the vertebral body. The influence of the upright position in the production of spondylolisthesis is emphasized. Attention is called to the loss of bony continuity at the isthmus (pars interarticularis) of the laminæ and the loss of rigid support at the base of the vertebral column. After a very thorough portrayal of the clinical manifestations of this condition, the author describes the methods of treatment and adds a surgical procedure of his own. This monograph is well illustrated with many diagrams, photographs, and roentgenograms. An excellent résumé of the subject of spondylolisthesis to the present date.

FREMONT A. CHANDLER.

A DISTINCT need in experimental pathology has been filled in the small volume[2] by Wagoner and Custer. The frontispiece is a portrait of Julius Friederich Cohnheim, "the most eminent of Virchow's pupils," who "by brilliant experiments on living animals . . . revivified a pedantic subject and demonstrated to others a method of investigation which, in a few brief years, has yielded incalculable benefits to mankind." The book is divided into three sections. The first deals with surgical technique and experimental methods, anæsthetization of the experimental animals, general care of the experimental animal, and normal blood findings in laboratory animals. The general principles of surgical technique are briefly but adequately described, and the different types of knots and sutures are well illustrated. The necessity of care in anæsthetization is strongly emphasized. In the foreword Professor Krumbhaar remarks, "except for the appalling ignorance in some non-medical circles of the conditions under which animal experimentation is carried on, it would be unnecessary to mention that absolute asepsis, general anæsthesia, and similar precautions are carried out wherever indicated, with as strict conscientiousness as in the human operating clinic—in fact, such conditions are usually essential to the success of the experiment as well as obligatory from humane points of view." The second and third sections are concerned with methods of producing general pathological conditions and lesions of special organs. One hundred and nineteen experiments are described clearly and in such adequate detail that they can be carried out by any intelligent student. Most of the procedures for inducing pathological conditions have been well selected. Many of the more complicated methods, such as Mann's technique for inducing gastric ulcer by various types of gastric and intestinal anastomoses, have been omitted. The typography is excellent. Large, clear type and heavy unglazed paper render reading easy. The binding in heavy brown Holliston book duck is admirable for rough use in a laboratory. Following the descriptions of many experiments one or more references are given to important papers which will aid the student in technique and, especially, in interpreting his results. As there is no book of similar scope in English, this volume will be welcomed by teachers who wish to introduce their students to the field of experimental pathology either as a special elective course or as an accessory to the routine teaching of general and special pathology. J. P. SIMONDS.

THE book[3] by Crile and his associates is not a formal treatise on the thyroid gland but, as its preface states, is an account of the experience of the staff of the Cleveland Clinic in the treatment of diseases of that organ. In a sense then it is a binding together of many small articles—some profound, others very superficial. Dr. George Crile, Jr., writes the chapter on iodine and the thyroid gland; Dr. D. Roy McCullagh a short summary of the biochemistry of iodine. Dr. Crile writes on the rôle of the thyroid gland in the energy system, on endemic goiter, and on the mechanism of hyper- and hypothyroidism. Dr. Charles L. Hartsock discusses clinical aspects of hypothyroidism; Drs. Tucker and McDonald briefly describe the diagnosis of hyperthyroidism. Dr. E. Perry McCullagh writes a valuable chapter on the differential diagnosis of hyperthyroidism. Dr. Robert S. Dinsmore writes briefly on hyperthyroidism in children. No careful analysis of the physiologic results in this interesting field is given. Dr. John P. Anderson writes briefly on cardiac disturbances associated with hyperthyroidism. Two good articles are those by Dr. A. D. Ruedemann on ocular changes in hyperthyroidism, and by Henry J. John on carbohydrate metabolism in hyperthyroidism. A valuable treatise on roentgenological observations in thyroid disease by Dr. Bernard H. Nichols, well illustrated with X-ray films, serves to

[1] LE SPONDYLOLISTHÉSIS. By Marc Antonin Azema. Paris: Jouve and Company, 1932.

[2] A HANDBOOK OF EXPERIMENTAL PATHOLOGY. By George Wagoner, M.D., and R. Philip Custer, M.D. With a foreword by Edward Bell Krumbhaar. Springfield, Illinois: Charles C. Thomas.

[3] DIAGNOSIS AND TREATMENT OF DISEASES OF THE THYROID GLAND. By George Crile and Associates. Philadelphia and London: W. B. Saunders Company, 1932.

emphasize the importance of substernal goiter. Malignant and inflammatory conditions of the thyroid are discussed in a series of chapters. Operative technique is described and illustrated by Dr. Dinsmore; special considerations in the technique are discussed in a separate chapter by Dr. Crile. The diagnosis and treatment of parathyroid tetany is covered in a good chapter by Dr. E. Perry McCullagh. The book concludes with a short chapter on end-results of operations for hyperthyroidism by Dr. George Crile.

On the whole the book is, of course, interesting and a variety of illuminating studies from unusual angles are gathered together here. In general, however, one would conclude that most of these studies are too brief and too superficial to be of much value. The book is of interest to the student of thyroid diseases but not the authoritative treatise with which one would begin the study of those disorders.

PAUL STARR.

A BRIEF review of the most important advances in obstetrics and gynecology published in the past few years is contained in the third edition of the book[1] of Bourne and Williams. The book is written in a simple and direct manner, as a coherent text and not merely as a collection of abstracts. New material has been added on the subjects of anæsthetics in labor, carcinoma of the cervix, and functional uterine hæmorrhage. There is also a chapter on the X-ray in obstetrics and gynecology which is illustrated with excellent prints. The book bears evidence of thorough revision of previous editions and will prove valuable to the physician who wishes to keep abreast with the growing literature.

IRVING F. STEIN.

THE work[2] of Wuerdemann now in its second edition is still the only book in English, since that of Ramsay in 1907, devoted to the subject of injuries of the eye. The text has not been materially lengthened, and the number of illustrations has been reduced by more than one hundred. Those which are retained are of good quality, however, and are for the most part original. The paper and type of the present edition are excellent, a great improvement in these respects over the first edition.

The author shows his familiarity with the German and French literature and acknowledges his debt to the large work of Wagenmann. He has also drawn from a large personal experience and many of the conditions described are illustrated by case histories, giving treatment and results. In removing foreign bodies from the eye by the electro-magnet, the author prefers the anterior route, as a rule, by which the body is drawn around the lens into the anterior chamber, whence it is removed by corneal incision. The importance of X-rays in every case of suspected or even possible foreign body is emphasized.

Eighty pages are devoted to medicolegal questions, including important legal decisions and an abstract of the Workmen's Compensation Laws of the various states as they affect ocular injuries. Under these laws, compensation for loss of both eyes (total disability) varies from one thousand dollars (Georgia) to fifteen thousand dollars (South Dakota) averaging six thousand dollars. That for loss of one eye varies from six hundred dollars to two thousand, eight hundred and eighty dollars, averaging about two thousand dollars.

One misses from this book a consideration of some important recent work. Nothing is said about injuries with tear gas, especially as to the use of sodium sulphite in glycerine as a solvent, which was described by McNally. In considering enucleation of the globe and its substitutes, no mention is made of simple evisceration with retention of the cornea, an exceedingly valuable procedure. The operation described by the author is the old one with removal of the cornea, to which his disparaging remarks may well apply.

SANFORD R. GIFFORD.

THE monograph[3] on acromegaly by Atkinson is one of those concise but exhaustive collections dealing with a particular disease that no one interested in the subject can afford to be without. It is a straightforward presentation of all the reported findings, gathered from an exhaustive analysis of the world's literature. It consists of two main parts—a series of chapters presenting the findings of different authors concerning the historical, clinical, pathological, diagnostic, and therapeutic aspects of the disease, and a series of analytical tables covering the results of removal of the pituitary gland, the postmortem findings, the eye findings, a tabulation of certain features of the 1,319 cases that the author has collected from the literature, and finally a bibliography covering 63 pages. I am impressed with the thoroughness and clearness with which this review is presented.

PAUL STARR.

[1] RECENT ADVANCES IN OBSTETRICS AND GYNÆCOLOGY. By Aleck W. Bourne, M.A., M.B., B.Ch. (Camb.), F.R.C.S. (Eng.), F.C.O.G., and Leslie W. Williams, M.D., M.S. (Lond.), F.R.C.S. (Eng.), M. C. O. 3d ed. Philadelphia: P. Blakiston's Son and Co. Inc., 1932.

[2] INJURIES OF THE EYE; DIAGNOSIS AND TREATMENT, FORENSIC PROCEDURES AND VISUAL ECONOMIES. By Harry Vanderbilt Wuerdemann, M.D., Sc.D., F.A.C.S. 2d ed. St. Louis: The C. V. Mosby Company, 1932.

[3] ACROMEGALY. By F. R. B. Atkinson, M.D., C.M. (Edin.). With a foreword by Sir Arthur Keith. London: John Bale, Sons & Danielsson, Ltd., 1932.

BOOKS RECEIVED

Books received are acknowledged in this department, and such acknowledgment must be regarded as a sufficient return for the courtesy of the sender. Selections will be made for review in the interests of our readers and as space permits.

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THE PRINCIPLES AND PRACTICE OF OBSTETRICS. By Joseph B. DeLee, A.M., M.D. 6th thor. rev. ed. Philadelphia and London: W. B. Saunders Company, 1933.

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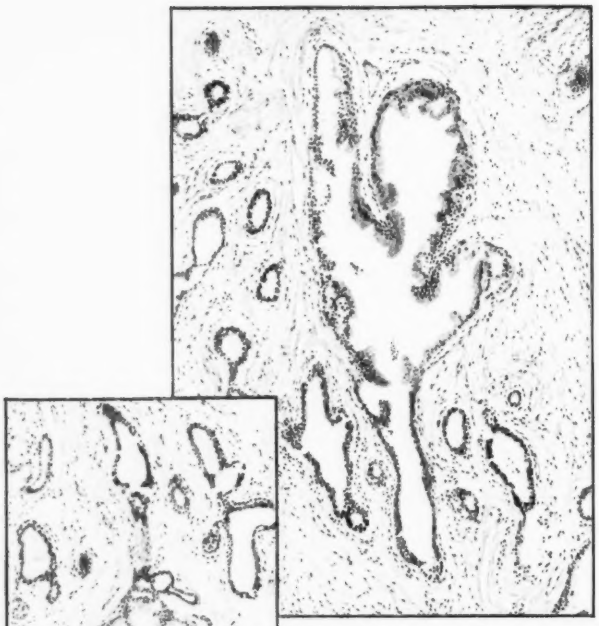

Fig. 4. Serial sections through an anastomosis of a sweat gland duct (apocrine type) with a lacteal duct of the breast.

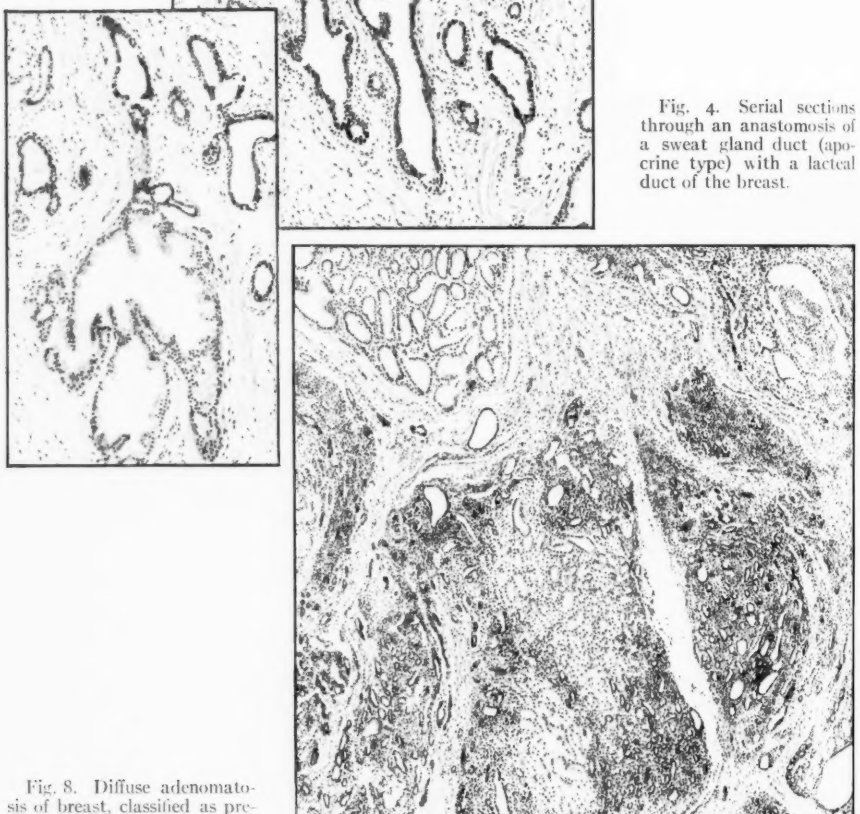

Fig. 8. Diffuse adenomatosis of breast, classified as precancerous.

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